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FILE CONTENT:1840 - 21 Jan 2007 VOL 146 ISS 4

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*                                                          *
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*                                                          *
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This file contains CAS Registry Numbers for easy and accurate substance
identification.

=> d que
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L2          104 SEA FILE=CASREACT SSS FUL L1 (   444 REACTIONS)


=> d l2 1-104 ibib abs fcrd


L2   ANSWER 1 OF 104  CASREACT  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        145:438615  CASREACT
TITLE:                   Enantioselective production of benzimidazole
                         derivatives and their salts
INVENTOR(S):             Jiang, Biao; Zhao, Xiao-Long; Dong, Jia-Jia; Wang,
                         Wan-Jun
PATENT ASSIGNEE(S):      Ratiopharm GmbH, Germany
SOURCE:                  Ger., 16pp.
                         CODEN: GWXXAW
DOCUMENT TYPE:           Patent
LANGUAGE:                German
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     DE 102005061720    B3   20061019       DE 2005-102005061720 20051222
PRIORITY APPLN. INFO.:                     DE 2005-102005061720 20051222
OTHER SOURCE(S):         MARPAT 145:438615
GI
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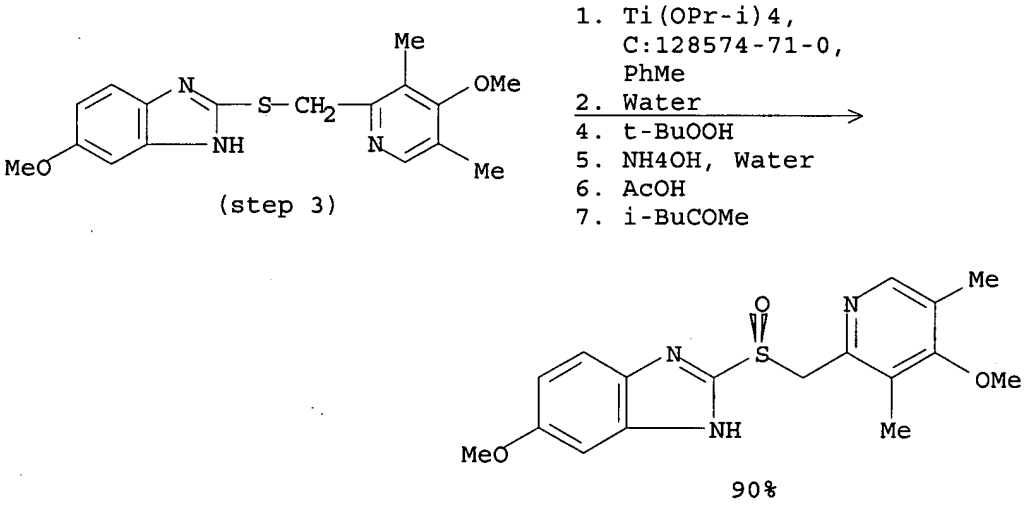
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention concerns a new procedure for the production of benzimidazole derivs. I with a chiral sulfoxide group in enantiomerically pure form or in a form, in which one of the two enantiomers is enriched opposite the other enantiomer. The invention concerns likewise a procedure for the production of the salts of the individual enantiomers of the benzimidazole derivs. with a chiral sulfoxide group. In particular the invention concerns a procedure for the production of the S-enantiomer of omeprazol (also known as esomeprazol) and the salts of it, in particular the zinc salt of the S-enantiomer of the omeprazol. The procedure comprises: (a) mix (R,R)- or (S,S)-1,2-bisarylethane-1,2-diols with titanium alkoxide in an organic solvent; (b) add water; (c) add a prochiral sulfide II; (d) add an oxidizing agent; (e) add aqueous ammonia; (f) add an acid; (g) extract with an organic solvent; (h) cool the organic solution and filter; and (i) optionally prepare the zinc salts of I. Thus, (S)-omeprazol (III) was prepared in 94 % yield and >99% enantiomeric excess from 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]thio]-1H-benzimidazole (IV) via S-oxidation with Me3COOH in aqueous PhMe containing Ti(OCHMe2)4 and (R,R)-1,2-bis(2-bromophenyl)ethane-1,2-diol.

RX(1) OF 5



NOTE: stereoselective (94% e.e.)
CON: STAGE(1) 10 minutes, 25 deg C
STAGE(2) 10 minutes, 25 deg C
STAGE(3) 25 deg C; 25 deg C -> -20 deg C
STAGE(4) 12 hours, -20 deg C
STAGE(5) -20 deg C -> room temperature
STAGE(6) room temperature; room temperature -> -10 deg C
STAGE(7) overnight, -10 deg C

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:377342 CASREACT
TITLE: Methoxylation process for the preparation of pantoprazole
INVENTOR(S): Palomo Nicolau, Francisco; Molina Ponce, Andres
PATENT ASSIGNEE(S): Quimica Sintetica, S. A., Spain

SOURCE: PCT Int. Appl., 22pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006100243	A1	20060928	WO 2006-EP60917	20060321

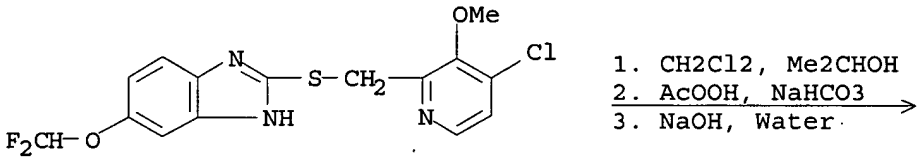
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

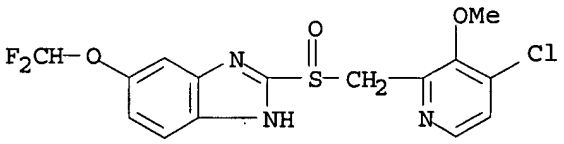
PRIORITY APPLN. INFO.: ES 2005-717 20050322

AB In the title process, the introduction of the methoxy group is carried over the position 4 of the pyridine ring of compound by substitution of the chlorine atom in the precursor mol. by reaction with an alkaline metal methoxide (e.g., sodium methoxide) in a mixture of methanol and an aprotic polar solvent (e.g., THF).

RX(1) OF 3



(step 1)



85%

NOTE: 0.1% of sulfone also detected
CON: STAGE(1) room temperature; room temperature -> 5 deg C
STAGE(2) 0 - 5 deg C
STAGE(3) pH 7.5 - 8.5

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:249204 CASREACT
TITLE: Process for preparation of (S)-omeprazole by enantioselective oxidation
INVENTOR(S): Jiang, Biao; Zhao, Xiaolong; Wang, Wanjun; Dong, Jiajia; Xu, Xiangya

10/542,268

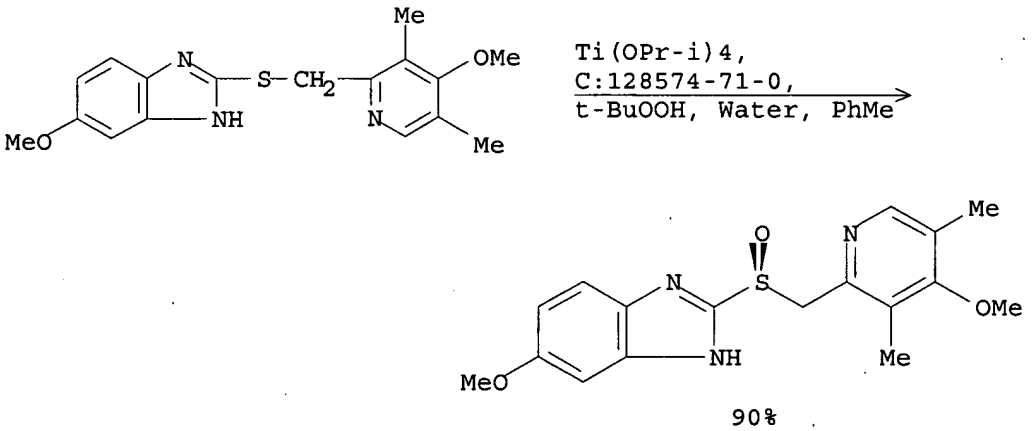
PATENT ASSIGNEE(S): Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 13pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1810803	A	20060802	CN 2006-10023955	20060217

PRIORITY APPLN. INFO.: CN 2006-10023955 20060217

AB The title method includes oxidizing 5-methoxy-2-(4-methoxy-3,5-dimethylpyridin-2-ylmethylthio)-1H-benzimidazole with oxidant in the presence of chiral bidentate ligand (R,R)/(S,S)-1,2-diaryl-ethylene glycol and titanium tetraalkoxide at a molar ratio of 1:(0.5-3):(0.02-0.4):(0.01-0.2) at -78°C to 50°C for 1-24 h; quenching reaction with basic aqueous solution and purifying to obtain neutral free base (S)-omeprazole solid with ee of 92-99%; wherein the chiral bidentate ligand and the titanium tetraalkoxide in-situ form a complex catalyst in the reaction; and the oxidant is a peroxide compound This invention has the advantages of no requirement for costly cumenyl hydroperoxide and diisopropylethylamine, and high yield.

RX(1) OF 2



90%

NOTE: stereoselective, ee 94%, optimization study, optimized on solvent, stoichiometry, reagent, temperature, catalyst
CON: STAGE(1) room temperature -> -20 deg C; 12 hours, -20 deg C

L2 ANSWER 4 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:152725 CASREACT
TITLE: Process for preparing lansoprazole
INVENTOR(S): Kotar-Jordan, Berta; Vrecer, Franc; Segula Zakelj, Mojca; Ritlop, Gregor
PATENT ASSIGNEE(S): Krka, Tovarna Zdravil, D.D., Novo Mesto, Slovenia
SOURCE: PCT Int. Appl., 51 pp. CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006074952	A1	20060720	WO 2006-EP285	20060113

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

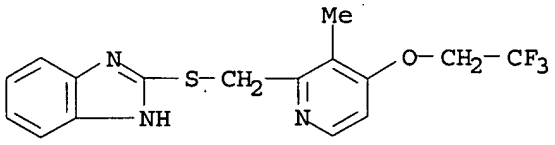
EP 1681056	A1	20060719	EP 2005-663	20050114

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

PRIORITY APPLN. INFO.:	EP 2005-663	20050114
	US 2005-269211	20051108

AB The invention relates to a process for preparing lansoprazole. It is also directed to lansoprazole having a sp. surface area and a pharmaceutical composition comprising lansoprazole. For example, polyvinylpyrrolidone K-30 66.0 g were dissolved in of purified water 500.0 g. Disodium hydrogen phosphate dihydrate 57.8 g were dissolved in purified water 500.0 g and then added to the solution of polyvinylpyrrolidone. Then, lansoprazole 247.5 g, sucrose 279.7 g and maize starch 174.0 g were added to the resulting solution and this dispersion was homogenized with an appropriate mixer/ homogenizer until a substantially homogeneous suspension was obtained. Finally, sodium dodecyl sulfate 25.0 g were dissolved in purified water 160.0 g and added into the suspension while gently stirring. The obtained suspension was then sprayed onto 1100.00 g of inert cores in a Wurster fluidized-bed equipment to form cores having a first layer. Such coated cores were addnl. coated with a dispersion containing 1500.0 g of Eudragit L-30D, 45.0 g of polyethylene glycol 6000, 144.0 g of talc, 43.5 g of titanium dioxide and 1500.0 g of water.

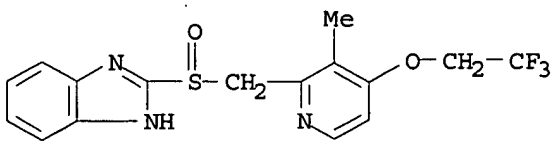
RX(11) OF 64



1. C:5588-84-1, NMEP
2. R:35220-04-3
3. Et3N, R:10102-17-7, Water

x H_2O

(step 1)



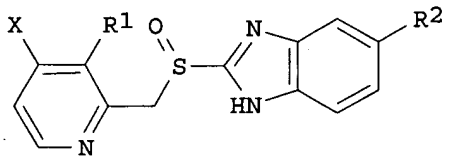
NOTE: optimization study
CON: STAGE(1) room temperature -> 0 deg C
STAGE(2) 0.5 hours, 0 - 10 deg C; 10 - 15 deg C

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:145705 CASREACT
TITLE: Process for preparation of benzimidazole derivatives
INVENTOR(S): Zhong, Huijuan
PATENT ASSIGNEE(S): Jiangsu Hansoh Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 12 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1789251	A	20060621	CN 2004-10066061	20041216

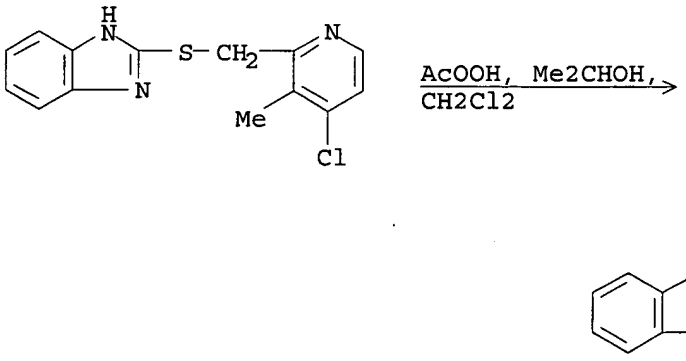
PRIORITY APPLN. INFO.: CN 2004-10066061 20041216
GI



I

AB This invention relates to a method for preparation of benzimidazole derivs. I [wherein X = halo or alkoxy; R1 = alkyl or alkoxy; R2 = H or (un)substituted alkoxy] in aprotic solvent in the presence of base. The aprotic solvent comprises DMF, DMSO, 2-butanone, and tetrahydrofuran; the base comprises sodium hydride, potassium tert-butoxide, sodium, sodium hydroxide, potassium hydroxide, and diisopropylethylamine.

RX(2) OF 6



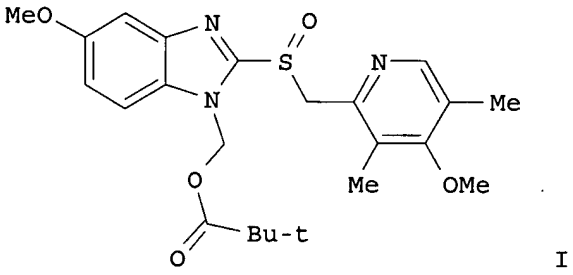
CON: STAGE(1) room temperature -> 10 deg C; <15 deg C; 0.5 hours, <15 deg C

L2 ANSWER 6 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:124565 CASREACT
TITLE: Preparation of benzimidazole derivatives as antiulcer

	agents for treatment of stomach and intestinal diseases
INVENTOR(S):	Zhong, Huijuan; Lu, Aifeng
PATENT ASSIGNEE(S):	Jiangsu Hansoh Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE:	Faming Zhuanli Shenqing Gongkai Shuomingshu, 24 pp. CODEN: CNXXEV
DOCUMENT TYPE:	Patent
LANGUAGE:	Chinese
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1754879	A	20060405	CN 2004-10081029	20040930
PRIORITY APPLN. INFO.:			CN 2004-10081029	20040930

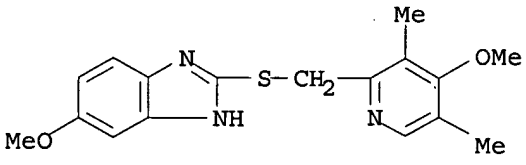
GI



I

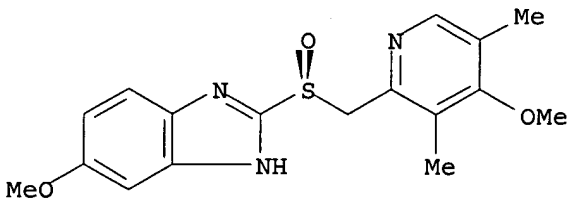
AB The title benzimidazole derivs. with general formula of R1-X-CO2-CH2-R2 [wherein X = O or a bond; R1 = (un)substituted alkyl, alkenyl, or alkynyl; R2 = substituted heteroring particularly benzimidazole] or pharmaceutically acceptable salts thereof were prepared as antiulcer agents for treating stomach and intestinal diseases. For example, I was prepared by reacting the corresponding benzimidazol-1-yl-methanol with pivaloyl chloride. I showed excellent antiulcer activity.

RX(1) OF 33



(step 1)

1. R:50740-42-6, Di-i-Pr D-tartrate, Water, PhMe
2. R:80-43-3, EtN(Pr-i)2
3. NH3, Water



NOTE: stereoselective
CON: STAGE(1) 54 deg C; 50 minutes, 54 deg C
STAGE(2) 1 hour, 30 deg C

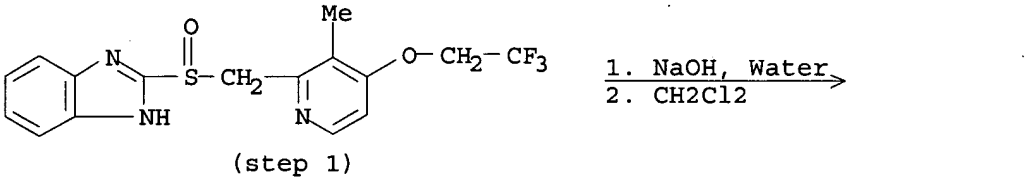
L2 ANSWER 7 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:62898 CASREACT
TITLE: Preparation of lansoprazole sodium as antiulcer agents
INVENTOR(S): Li, Haochao; Wang, Xiaoqin; Li, Zhongqiang; Bai, Jinlong; Ye, Hongyan
PATENT ASSIGNEE(S): Zhengzhou Bowei Medicine Science And Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 11 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1683367	A	20051019	CN 2005-10017379	20050225

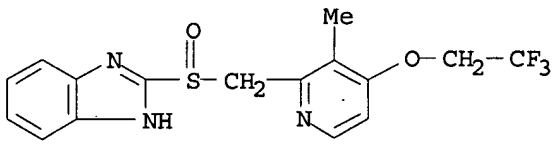
PRIORITY APPLN. INFO.: CN 2005-10017379 20050225

AB The title lansoprazole sodium was prepared as antiulcer agents for the treatment of gastric acid secretion, digestive tract ulcer, gastritis, etc. (no data). For example, lansoprazole acid was treated with 33% sodium hydroxide aqueous solution in isopropanol at room temperature to give lansoprazole sodium with 99.88% purity (92%). The title compound showed no allergy, hemolysis, and hemagglutination. Composition of lansoprazole sodium with meglumine, mannitol and water as injectable powder was described.

RX(1) OF 4



(step 1)



Na
90%

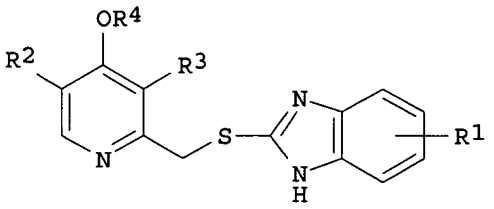
CON: STAGE(1) 5 minutes, room temperature
STAGE(2) 10 minutes, room temperature

L2 ANSWER 8 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:62896 CASREACT
TITLE: Process for preparing 2-(2-pyridylmethylsulfinyl)benzimidazoles via catalytic oxidation of the corresponding thioethers in the presence of molybdenum(II) acetylacetonate.
INVENTOR(S): Chen, Chih-Hung
PATENT ASSIGNEE(S): Industrial Technology Research Institute, Taiwan; Syn-Tech Chem & Pharm Co., Ltd.

SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006128964	A1	20060615	US 2005-115160	20050427
US 7064213	B2	20060620		

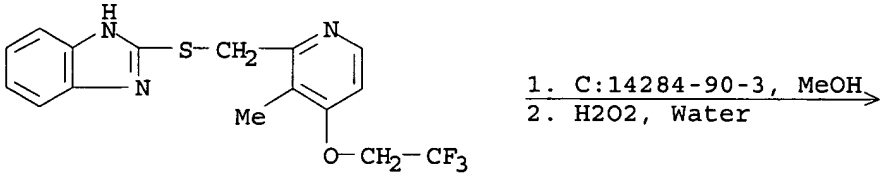
PRIORITY APPLN. INFO.: TW 2004-93138386 20041210
OTHER SOURCE(S): MARPAT 145:62896
GI



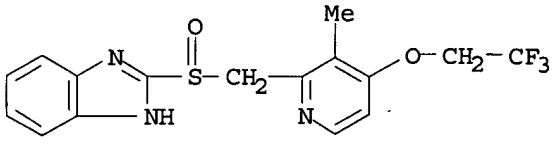
I

AB Title compds. (I; R1 = H, halo, alkyl, alkoxy, haloalkoxy; R2, R3 = H, halo, alkyl, alkoxy, haloalkyl, haloalkoxy; R4 = H, alkyl, haloalkyl), were prepared via oxidation of the corresponding thioethers in the presence of catalytic Mo(II) acetylacetonate in a solvent. Thus, 5-methoxy-2-[(4-methoxy-3,5-dimethyl-2-pyridyl)methylthio]-1H-benzimidazole, Bu4NBr, and Mo(acac)2 in MeOH at 0-5° were treated with 35% aqueous H2O2 to give after 2 h 91-92% Omeprazole of >98% purity.

RX(2) OF 3



(step 1)



92%

NOTE: optimization study(optimized on solvent, temperature)
CON: STAGE(1) room temperature -> 5 deg C
STAGE(2) 2 hours, 0 - 5 deg C

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:27912 CASREACT
TITLE: Identification and synthesis of potential impurities

of rabeprazole sodium

AUTHOR(S): Pingili, R. Reddy; Jambula, M. Reddy; Ganta, M. Reddy; Ghanta, M. Reddy; Sajja, E.; Sundaram, V.; Boluggdu, V. Bhaskar

CORPORATE SOURCE: Department of Research and Development, Dr. Reddy's Laboratories Ltd., Bollaram, India

SOURCE: Pharmazie (2005), 60(11), 814-818
CODEN: PHARAT; ISSN: 0031-7144

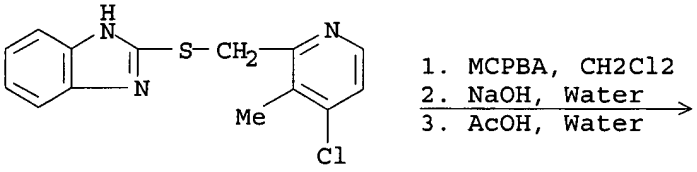
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

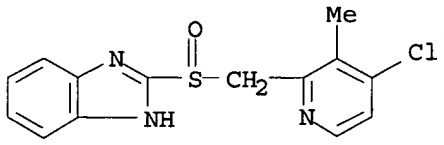
AB Rabeprazole sodium (I, Achiphex) is a gastric proton pump inhibitor. It causes dose-dependent inhibition of acid secretion and is useful as an anti-ulcer agent. In the process for the preparation of I, two potential unknown impurities were identified in HPLC at levels ranging from 0.05-0.8%. Based on mass spectral data vide LC-MS, the two impurities were characterized as 2-{[(4-chloro-3-methyl-2-pyridinyl)methyl]sulfinyl}-1H-benzimidazole (II, chloro analog of rabeprazole) and 2-[{(4-methoxy-3-methyl-2-pyridinyl)methyl}sulfinyl]-1H-benzimidazole (III, methoxy analog of rabeprazole). The structures were unambiguously established by independently synthesizing them and co-injecting in HPLC. To our knowledge, the compds. II and III have not been reported as process impurities elsewhere.

RX(1) OF 48



1. MCPBA, CH2Cl2
2. NaOH, Water
3. AcOH, Water

(step 1)



60%

CON: STAGE(1) 1 hour, -10 - -15 deg C
STAGE(3) pH 8.0 - 8.5

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 144:390922 CASREACT

TITLE: Stereoselective oxidation processes for the preparation of chiral substituted sulfoxides from the racemic sulfides

INVENTOR(S): Kumar, Neela Praveen; Khanna, Mahavir Singh; Prasad, Mohan; Kumar, Yatendra

PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India

SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006040635	A1	20060420	WO 2005-IB2946	20051004

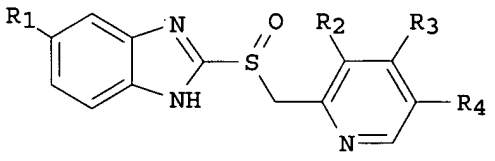
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

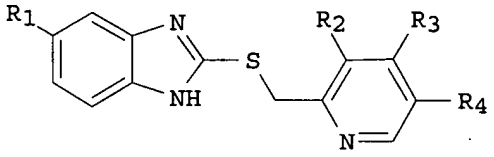
PRIORITY APPLN. INFO.: IN 2004-DE1957 20041011

OTHER SOURCE(S): MARPAT 144:390922

GI



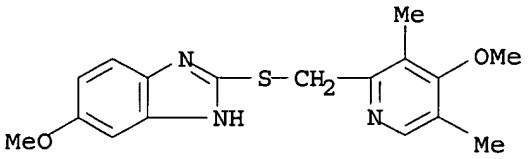
I



II

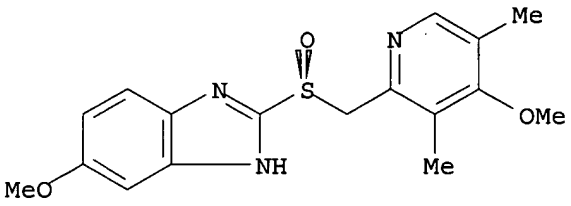
AB An enantioselective catalytic oxidation process for the preparation of an optically active enantiomer or an enantiomerically enriched form of a substituted pyridinylmethylsulfinylbenzimidazole [I; R1-R4 = H, C1-4 (un)branched alkyl, C1-4 (un)branched alkoxy, aryl, aryloxy], or its pharmaceutically acceptable salts (e.g., esomeprazole potassium), comprises oxidizing a prochiral sulfide (II; e.g., omeprazole sulfide) in the presence of a chiral transition metal complex [e.g., titanium isopropoxide and L-(+)-diethyl tartrate] and a base (e.g., diisopropylethylamine) in the absence of an organic solvent with an oxidant (e.g., cumene hydroperoxide) followed by an optional salification (e.g., potassium hydroxide).

RX(1) OF 3



(step 2)

1. Ti(OPr-i)4, Di-Et L-tartrate
2. Cumene hydroperoxide, Di-Et L-tartrate, EtN(Pr-i)2
3. KOH, MeOH



K

NOTE: optimization study, stereoselective
CON: STAGE(1) room temperature -> 50 deg C; 1.5 hours; 25 - 30 deg C
STAGE(2) 25 - 30 deg C; 3 hours, 25 - 30 deg C
STAGE(3) 25 - 35 deg C; 15 - 16 hours, 25 - 35 deg C

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:370097 CASREACT
TITLE: Liquid-phase oxidation process for the preparation and purification of pantoprazole sodium sesquihydrate from pantoprazole sulfide analog
INVENTOR(S): Chava, Satyanarayana; Gorantla, Seeta Ramanjaneyulu; Ginjupalli, Sai Prasanna Bhagya Lakshmi
PATENT ASSIGNEE(S): Matrix Laboratories Ltd, India
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

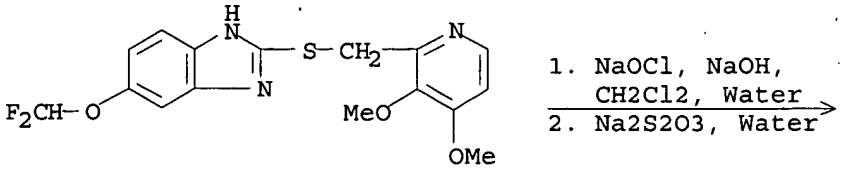
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006040778	A1	20060420	WO 2005-IN327	20050927

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

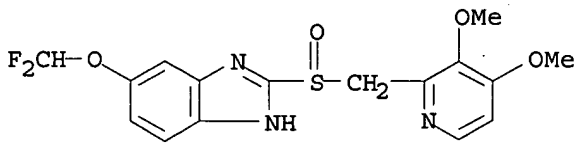
PRIORITY APPLN. INFO.: IN 2004-CH1076 20041015

AB A method is described for the liquid-phase oxidation of the pantoprazole sulfide analog with sodium hypochlorite in methylene chloride along with a process for the purification of pantoprazole sodium sesquihydrate.

RX(1) OF 1



(step 1)



67%

CON: STAGE(1) room temperature -> -2 deg C; 2.5 hours, -2 - 2 deg C; 1.5 hours, -2 - 0 deg C
STAGE(2) 0.5 hours, 0 - 10 deg C

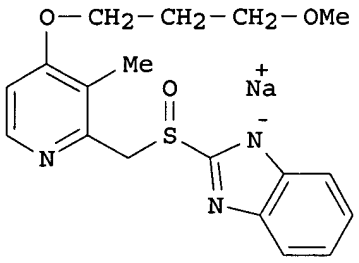
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:292755 CASREACT
TITLE: Preparation of an amorphous powder of sodium rabeprazole
INVENTOR(S): Venkatachalam, Raman; Dixit, Girish; Babu Prasad, Bangalore Raja Rao; Singh, Jitendra; Chahal, Arvinder Singh
PATENT ASSIGNEE(S): Apollo International Limited, India
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006024890	A1	20060309	WO 2004-IB2822	20040830

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

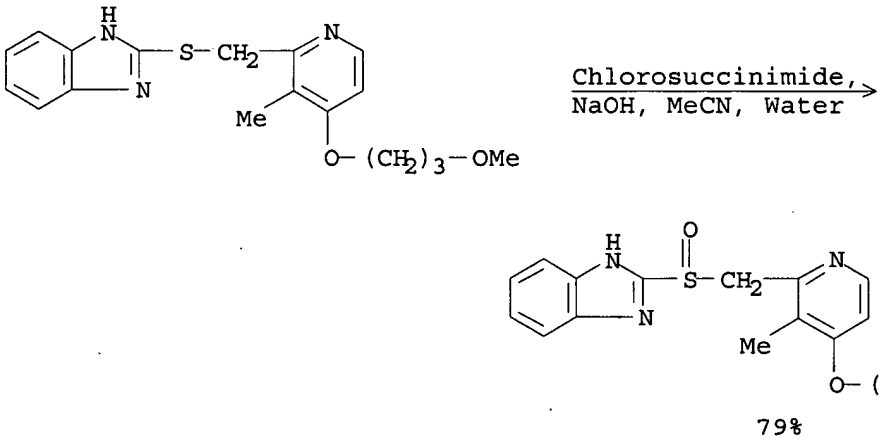
PRIORITY APPLN. INFO.: WO 2004-IB2822 20040830
GI



I

AB A process for the preparation of title compound I via the oxidation of rabeprazole
sulfide in non-aqueous solvents was disclosed. For example, MCPBA mediated oxidation of rabeprazole sulfide in dichloromethane, followed by a non-aqueous work-up afforded sodium rabeprazole. Of note, the disclosed process exclusively provides the sodium salt rabeprazole in non-aqueous solvents.

RX(1) OF 1



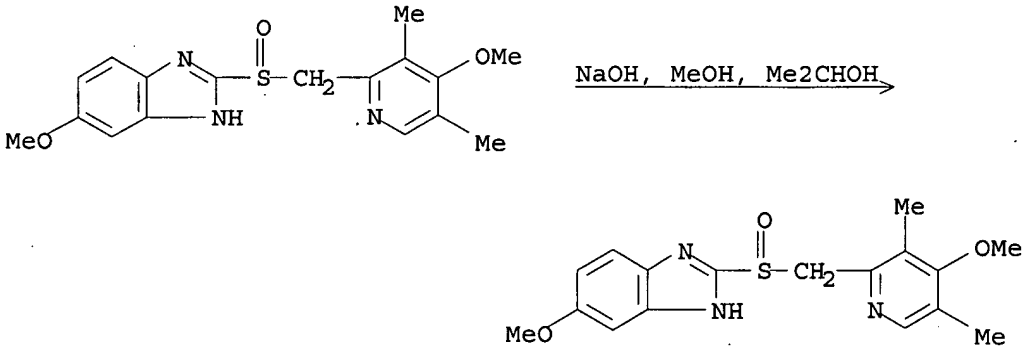
NOTE: optimization study
CON: STAGE(1) room temperature -> 5 deg C; 2 hours, 0 - 5 deg C

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:192176 CASREACT
TITLE: Preparation of Optically Pure Esomeprazole and Its Related Salt
AUTHOR(S): Raju, Satya V. N.; Purandhar, Koilkonda; Reddy, Padi Pratap; Reddy, Ghanta Mahesh; Reddy, Lekkala Amarnath; Reddy, Kikkuri Srirami; Sreenath, Keshaboina; Mukkanti, Kagga; Reddy, Ganji Santhi
CORPORATE SOURCE: Research and Development, Dr. Reddy's Laboratories Ltd., Bollaram, 502-325, India
SOURCE: Organic Process Research & Development (2006), 10(1), 33-35
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The magnesium salt of (S)-isomer of omeprazole, with a trade name of Nexium, is the first proton-pump inhibitor developed as a single isomer for the treatment of acid-related diseases. A process for the preparation of the optically pure (S)-isomer of omeprazole and its magnesium salt from the racemic compound via formation of a transition metal complex is described.

RX(1) OF 6



Na
95%

NOTE: scalable
CON: 1 - 2 hour, room temperature

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:51582 CASREACT
TITLE: Process for the preparation of pyridin-2-ylmethylsulfinyl-1H-benzimidazoles via oxidation of the corresponding sulfides in the presence of zirconium or hafnium complexes.
INVENTOR(S): Kohl, Bernhard; Mueller, Bernd; Weingart, Ralf Steffen
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005118569	A1	20051215	WO 2005-EP52471	20050531

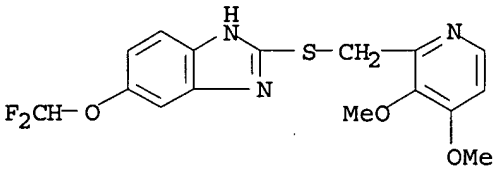
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2004-102467 20040602

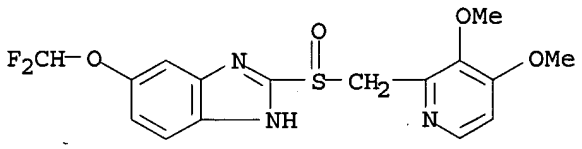
AB A process for preparing mixts. of enantiomers of proton pump inhibitors (PPIs) having a sulfinyl structure comprises oxidation of the corresponding sulfides in the presence of a mixture of enantiomers of chiral zirconium or hafnium complexes. Thus, 5-difluoromethoxy-2-[(3,4-dimethoxy-2-pyridinyl)methylthio]-1H-benzimidazole was heated with DL-tartaric acid bis(N-pyrrolidinamide) and zirconium tetra-n-propoxide in Me iso-Bu ketone at 40° for 1 h followed by addition of diisopropylethylamine and slow addition of cumene hydroperoxide to give 75% 5-difluoromethoxy-2-[(3,4-dimethoxy-2-pyridinyl)methylsulfinyl]-1H-benzimidazole.

RX(1) OF 1



(step 1)

1. C:23519-77-9, C:871366-86-8, i-BuCOMe, PrOH
2. Cumene hydroperoxide, EtN(Pr-i)2
3. Na2S2O3, NaHCO3, i-BuCOMe, Water



75%

NOTE: optimization study
CON: STAGE(1) 1 hour, 40 deg C; 40 deg C -> room temperature
STAGE(2) room temperature; 5 - 24 hours, room temperature

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 144:36340 CASREACT
TITLE: A novel stereoselective synthesis of benzimidazole sulfoxides
INVENTOR(S): Parthasaradhi Reddy, Bandi; Rathnakar Reddy, Kura; Raji Reddy, Rapolu; Muralidhara Reddy, Dasari
PATENT ASSIGNEE(S): Hetero Drugs Limited, India
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005116011	A1	20051208	WO 2004-IN143	20040528

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

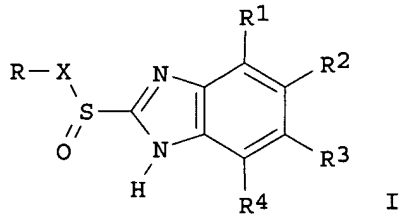
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2006166986 A1 20060727 US 2004-503846 20040806

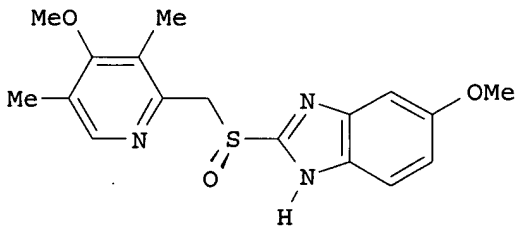
PRIORITY APPLN. INFO.: WO 2004-IN143 20040528

OTHER SOURCE(S): MARPAT 144:36340

GI



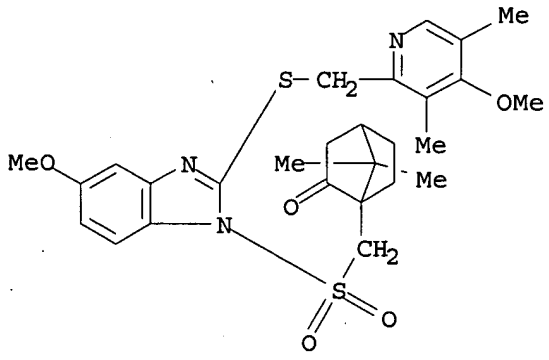
I



II

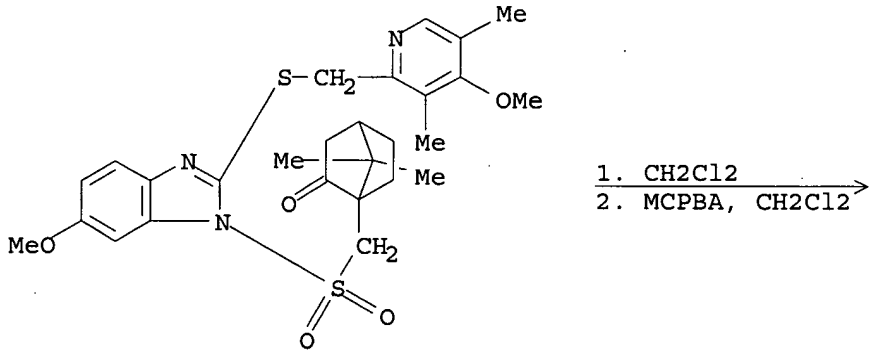
AB The present invention relates to a process for stereoselective synthesis of substituted sulfoxides of formula I [R = (un)substituted 2-pyridinyl; X = -CH(R5)- or (un)disubstituted-ortho-phenyl; R1,R2,R3,R4 = independently H, alkyl;, alkoxy, halogen, etc.; R5 = H or forms an alkylene chain together with R] either as a single enantiomer or in an enantiomerically enriched form. Thus, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]thio]-1H-benzimidazole is reacted with (R)-camphorsulfonyl chloride to form a mixture of 1-(R)-camphorsulfonyl-5-(and 6-)methoxy-2-[(3,5-dimethyl-4-methoxy-2-pyridyl)methylthio]-1H-benzimidazole, oxidized to obtain a diastereomeric excess of 1-(R)-camphorsulfonyl-(5- and 6-)-methoxy-2-[(3,5-dimethyl-4-methoxy-2-pyridyl)methyl-(S)-sulfinyl]-1H-benzimidazole over 1-(R)-camphorsulfonyl-(5- and 6-)-methoxy-2-[(3,5-dimethyl-4-methoxy-2-pyridyl)methyl-(R)-sulfinyl]-1H-benzimidazole. The diastereomers are separated by fractional crystallization and the separated 1-(R)-camphorsulfonyl-(5- and 6-)-methoxy-2-[(3,5-dimethyl-4-methoxy-2-pyridyl)methyl-(S)-sulfinyl]-1H-benzimidazole is deprotected to give (S)-esomeprazole (II).

RX(2) OF 24



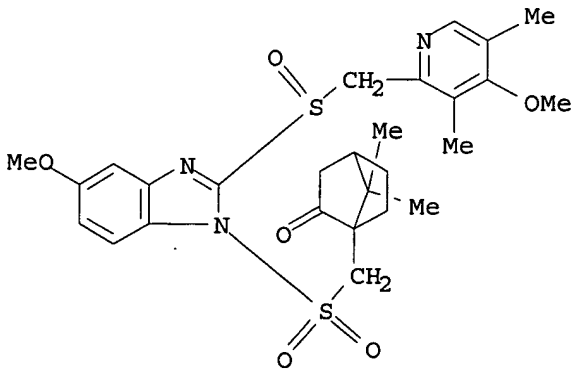
(step 1)

RX(2) OF 24

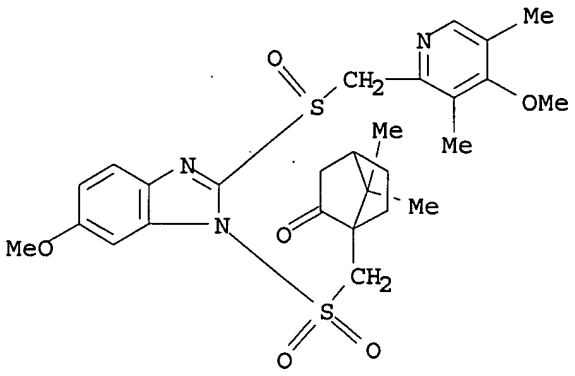


(step 1)

RX(2) OF 24



RX(2) OF 24



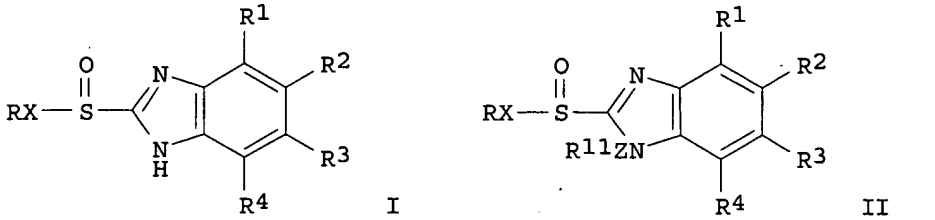
NOTE: dr 4.4:1, stereoselective
CON: STAGE(1) 30 - 35 deg C
STAGE(2) 30 minutes, -5 deg C; 3 hours, -5 deg C

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 16 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:460147 CASREACT
TITLE: process for preparing pyridinylmethyl benzimidazolyl sulfoxides in enantiomerically enriched form or as single enantiomers via separation of diastereomers
INVENTOR(S): Parthasaradhi Reddy, Bandi; Rathnakar Reddy, Kura; Raji Reddy, Rapolu; Muralidhara Reddy, Dasari
PATENT ASSIGNEE(S): Hetero Drugs Limited, India
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

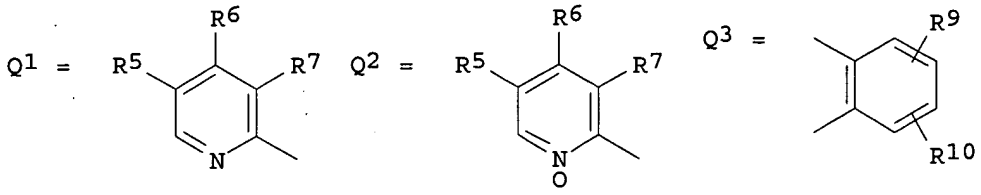
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005105786	A1	20051110	WO 2004-IN118	20040428
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1740571	A1	20070110	EP 2004-729974	20040428
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
US 2006089386	A1	20060427	US 2004-503830	20040806

PRIORITY APPLN. INFO.: WO 2004-IN118 20040428
OTHER SOURCE(S): MARPAT 143:460147
GI



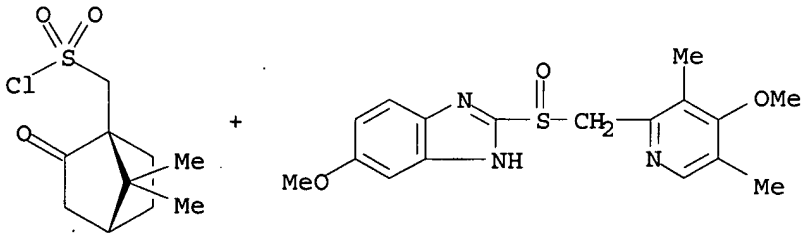
I

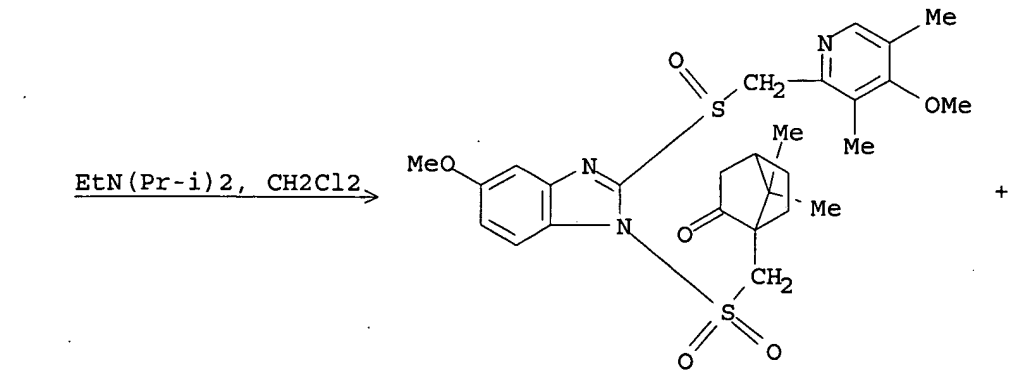
II



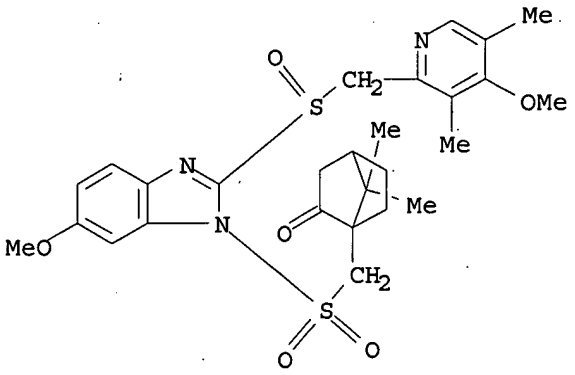
AB Single enantiomers or enantiomerically enriched mixts. of title compds. [I; R = Q1, Q2; X = CHR8, Q3; R1-R4 = H, alkyl, alkoxy, halo, haloalkoxy, alkylcarbonyl, alkoxycarbonyl, oxazolyl, CF3; adjacent R1-R4 form (substituted) ring structures; R5, R7 = H, alkyl, alkylthio, alkoxy, fluoroalkoxy, alkoxyalkoxy, dialkylamino, piperidino, morpholino, phenylalkyl, phenylalkoxy; R6 = R5, NO2; R8 = H; R7R8 = alkylene; R9, R10 = H, halo, alkyl], were prepared by reaction of racemic I with substantially enantiomerically pure R11ZY (R11 = chiral moiety with ≥1 asym. center; Z = SO2, SO, CO; Y = leaving group) to give diastereomers (II; variables as above) followed by separation of diastereomers and deprotection with acid or base followed by optional conversion to salts. Thus, racemic omeprazole reacted with (S)-camphorsulfonyl chloride to form a diastereomeric mixture and the diastereomers were separated by fractional crystallization from isopropanol, followed by cleavage with NaOH in MeOH/H2O to give esomeprazole.

RX(1) OF 10





RX(1) OF 10



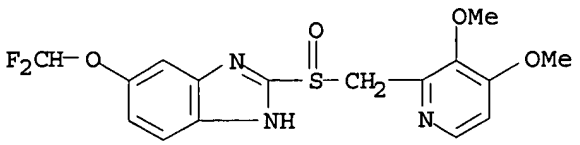
CON: STAGE(1) room temperature -> 5 deg C; 1 hour, 0 - 5 deg C;
3 hours, 0 - 5 deg C

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

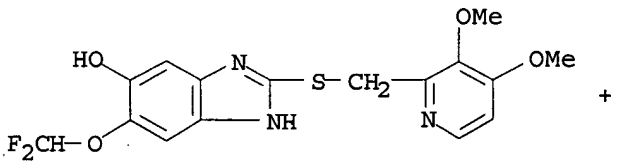
L2 ANSWER 17 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:404562 CASREACT
TITLE: Biotransformation of pantoprazole by the fungus Cunninghamella blakesleeana
AUTHOR(S): Xie, Z. Y.; Huang, H. H.; Zhong, D. F.
CORPORATE SOURCE: Laboratory of Drug Metabolism and Pharmacokinetics, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China
SOURCE: Xenobiotica (2005), 35(5), 467-477
CODEN: XENOBH; ISSN: 0049-8254
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To investigate the biotransformation of pantoprazole, a proton-pump inhibitor, by filamentous fungus and further to compare the similarities between microbial transformation and mammalian metabolism of pantoprazole, four strains of Cunninghamella (C. blakesleeana AS 3.153, C. echinulata AS 3.2004, C. elegans AS 3.156, and AS 3.2028) were screened for the ability to catalyze the biotransformation of pantoprazole. Pantoprazole was partially metabolized by four strains of Cunninghamella, and C. blakesleeana AS 3.153 was selected for further investigation. Three metabolites produced by C. blakesleeana AS 3.153 were isolated using semi-preparative HPLC, and their structures were identified by a combination anal. of LC/MSn and NMR spectra. Two further metabolites were confirmed with the aid of synthetic reference compds. The structure of a glucoside was tentatively assigned by its chromatog. behavior and mass spectroscopic data. These six metabolites were separated and quant. assayed by liquid chromatog.-ion trap mass spectrometry. After 96h of incubation with C. blakesleeana AS 3.153, approx. 92.5% of pantoprazole was metabolized to six metabolites: pantoprazole sulfone (M1, 1.7%), pantoprazole thioether (M2, 12.4%), 6-hydroxy-pantoprazole thioether (M3, 1.3%), 4'-O-demethyl-pantoprazole thioether (M4, 48.1%), pantoprazole thioether-1-N-β-glucoside (M5, 20.6%), and a glucoside conjugate of pantoprazole thioether (M6, 8.4%). Among them, M5 and M6 are novel metabolites. Four phase I metabolites of pantoprazole produced by C. blakesleeana were essentially similar to those obtained in mammals. C. blakesleeana could be a useful tool for generating the mammalian phase I metabolites of pantoprazole.

RX(1) OF 1



D-Glucose, K2HPO4, HCl, NaCl, Water



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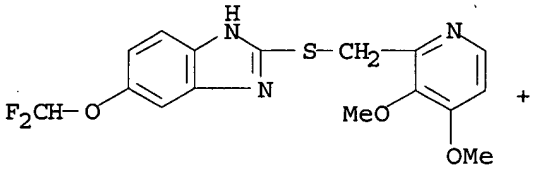
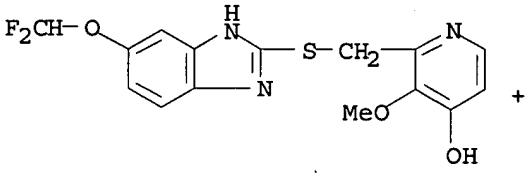
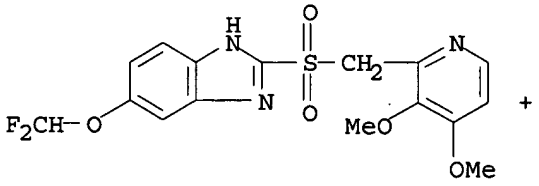


12%

RX(1) OF 1

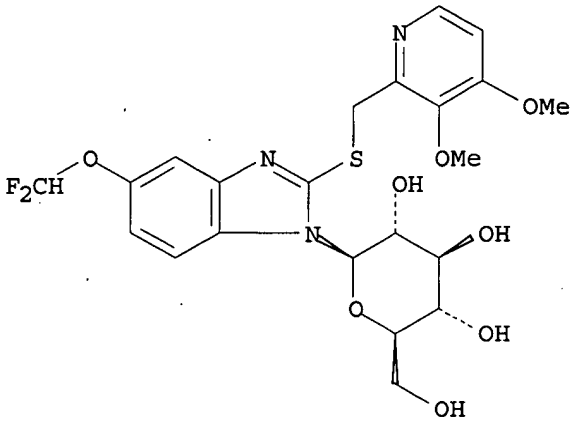


48%



2%

RX(1) OF 1



21%

NOTE: biotransformation, Cunninghamella blakesleeana used, described medium, other strains of Cunninghamella gave lower yield
CON: 96 hours, 25 deg C, pH 6.5

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

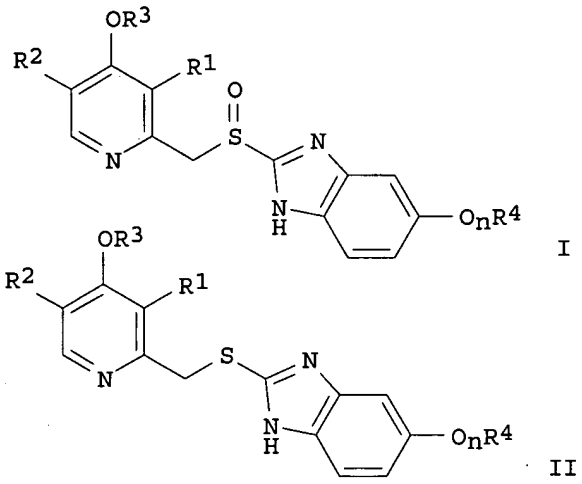
L2 ANSWER 18 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:286431 CASREACT
TITLE: Process for the preparation of sulfinyl derivatives by oxidation of the corresponding sulfides with hydrogen peroxide and rhenium catalyst
INVENTOR(S): Turchetta, Stefano; Massardo, Pietro; Tuozzi, Angela
PATENT ASSIGNEE(S): Chemi S.p.A., Italy
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056803	A1	20040708	WO 2002-IT200826	20021223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002368496	A1	20040714	AU 2002-368496	20021223
EP 1575935	A1	20050921	EP 2002-808286	20021223
EP 1575935	B1	20060524		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
AT 327233	T	20060615	AT 2002-808286	20021223
ES 2260522	T3	20061101	ES 2002-2808286	20021223
US 2006014798	A1	20060119	US 2005-149544	20050610
US 7105681	B2	20060912		

PRIORITY APPLN. INFO.: EP 2002-808286 20021223
WO 2002-IT826 20021223

OTHER SOURCE(S): MARPAT 143:286431

GI

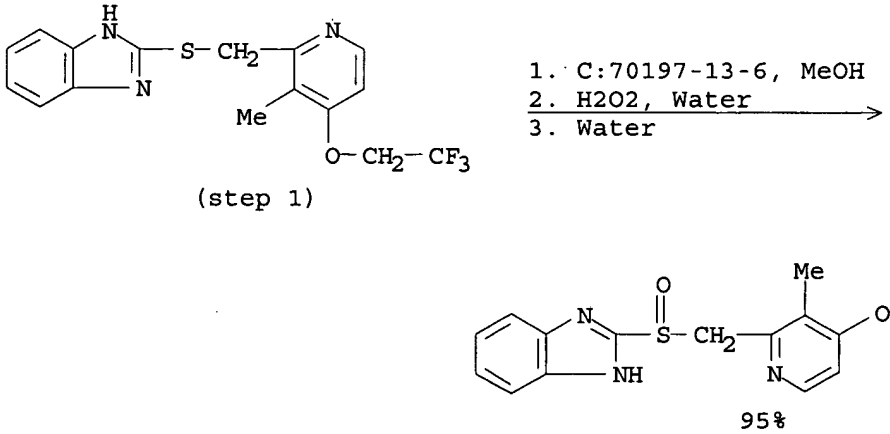


I

II

AB The present invention relates to a mild and industrially applicable process for preparing sulfinyl derivs. I (R1 = H, C1-4 alkyl, C1-4 alkoxy; R2 = H, C1-4 alkyl; R3 = C1-4 alkyl, fluorinated C1-4 alkyl, C1-4 alkoxy-C1-4 alkyl; R4 = H, C1-4 alkyl; n = 0, 1), useful as inhibitors of gastric acid secretion, comprising the selective oxidation of the corresponding sulfides II in which the oxidation is performed with H2O2 in the presence of low amts. of a rhenium compound as catalyst, at a temperature from 0° to room temperature Thus, treatment of 50 g (0.124 mol) lansoprazole sulfide (II; R1 = Me, R2 = R4 = H, R3 = CH2CF3, n = 0) with 127.8 g (0.173 mol) 33% aqueous H2O2 in 500 mL MeOH in the presence of 35 mg (0.00014 mol) methyltrioxorhenium at 5° for 4 h gave lansoprazole (I; R1 = Me, R2 = R4 = H, R3 = CH2CF3, n = 0) in 75% yield and >99.5% purity after recrystn.

RX(2) OF 6



(step 1)

95%

CON: STAGE(1) room temperature -> 5 deg C
STAGE(2) 4 hours, 5 deg C
STAGE(3) 1 hour, 5 deg C

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

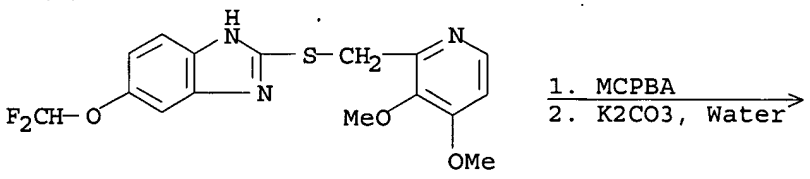
L2 ANSWER 19 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:235469 CASREACT
TITLE: Pyridinylbenzimidazole sulfoxides with high purity
INVENTOR(S): Uensal, Serafettin
PATENT ASSIGNEE(S): Ulkar Kimya Sanayii Ve Ticaret A. S., Turk.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077936	A1	20050825	WO 2004-EP1248	20040211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1716136	A1	20061102	EP 2004-710023	20040211
R: DE, TR				

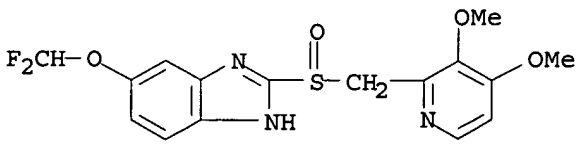
PRIORITY APPLN. INFO.: WO 2004-EP1248 20040211
OTHER SOURCE(S): MARPAT 143:235469

AB A method for preparing a pyridinylbenzimidazole sulfoxide consists of oxidizing a pyridybenzimidazole thioether with an oxidizing agent, and during the oxidation step a pyridinylbenzimidazole oxidizing sulfone compound is formed as an undesired byproduct. It is proposed to stop the oxidation step prior to the time when the amount of the undesired pyridinylbenzimidazolesulfone product exceeds 1.0 %-by weight

RX(2) OF 3



(step 1)



NOTE: other product also detected, pilot-plant scale
CON: STAGE(1) 8 hours, <-20 deg C
STAGE(2) -20 deg C -> room temperature; 30 minutes, room temperature; room temperature, pH 11.3

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 20 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:229857 CASREACT
TITLE: Preparation of new compounds useful for the synthesis of S- and R-omeprazole
INVENTOR(S): von Unge, Sverker; Fregler, Christina
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

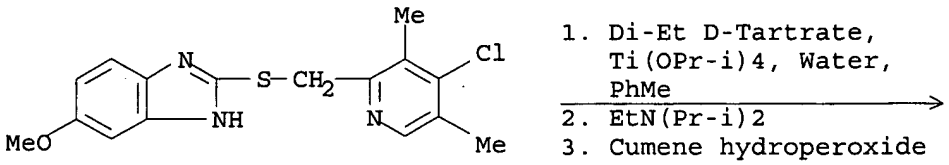
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005187256	A1	20050825	US 2005-60138	20050217
CA 2553877	A1	20050901	CA 2005-2553877	20050217
WO 2005080374	A1	20050901	WO 2005-SE221	20050217
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1718636	A1	20061108	EP 2005-711081	20050217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				

PRIORITY APPLN. INFO.: SE 2004-410 20040220
WO 2005-SE221 20050217

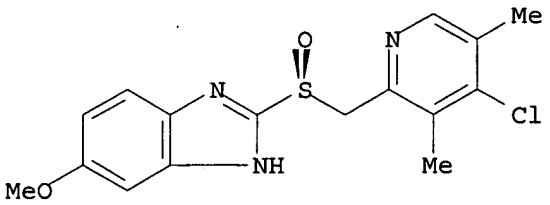
OTHER SOURCE(S): MARPAT 143:229857

AB The present invention relates to an improved method for the synthesis of the (S)- or (R)-enantiomer of omeprazole, characterized in that 2-[[(4-X-3,5-dimethylpyridin-2-yl)methyl]thio]-5-methoxy-1H-benzimidazole or 2-[[(4-X-3,5-dimethyl-1-oxidopyridin-2-yl)methyl]thio]-5-methoxy-1H-benzimidazole, wherein X is a leaving group, is oxidized into the corresponding sulfoxide which is obtained as a crystalline compound Recrystn. of the thus obtained sulfoxide results in a compound of enhanced chemical and optical purity, which is subsequently transformed into the (S)- or (R)-enantiomer of omeprazole. E.g., 2-[[(4-chloro-3,5-dimethylpyridin-2-yl)methyl]sulfinyl]-5-methoxy-1H-benzimidazole was prepared by treatment of 2-[[(4-chloro-3,5-dimethylpyridin-2-yl)methyl]thio]-5-methoxy-1H-benzimidazole with Ti(OPr-iso)4 in the presence of (S,S)-diethyl tartrate and then diisopropylethylamine and cumene hydroperoxide.

RX(1) OF 2



(step 1)



NOTE: stereoselective
CON: STAGE(1) room temperature; 0.5 hours, 50 deg C
STAGE(2) 15 minutes, room temperature
STAGE(3) 2 hours, room temperature

L2 ANSWER 21 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:59978 CASREACT
TITLE: A process for the preparation of substituted (pyridinylmethylsulfinyl)benzimidazole enantiomers
INVENTOR(S): Parthasaradhi Reddy, Bandi; Rathnakar Reddy, Kura; Raji Reddy, Rapolu; Muralidhara Reddy, Dasari
PATENT ASSIGNEE(S): Hetero Drugs Limited, India
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

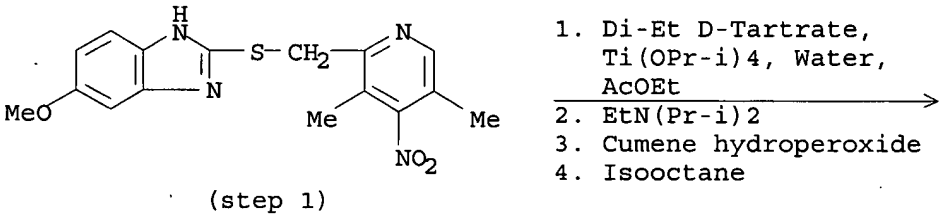
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005054228	A1	20050616	WO 2003-IN384	20031205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003288703	A1	20050624	AU 2003-288703	20031205
PRIORITY APPLN. INFO.:			WO 2003-IN384	20031205

OTHER SOURCE(S): MARPAT 143:59978
GI

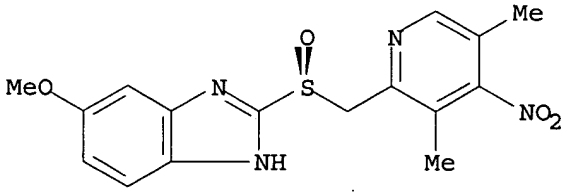
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides an enantioselective process for preparing substituted benzimidazoles I, such as omeprazole (II; R8 = OMe), either as a single enantiomer or in an enantiomerically enriched form, via oxidation with chiral Ti complexes. In compds. I, R1 and R2 are independently selected from H, alkyl, alkylthio, and (un)substituted alkoxy; R3 is alkyl optionally substituted with fluorine, alkoxyalkyl, or phenylalkyl; Y is O or S; and R4, R5, R6, and R7 are independently selected from H, alkyl, alkoxy, halo, haloalkoxy, alkylcarbonyl, alkoxycarbonyl, oxazolyl, and trifluoroalkyl. The process allows for the preparation of substituted 2-[(pyridin-2-yl)methylsulfinyl]benzimidazoles I in two steps from 2-[(4-nitropyridin-2-yl)methylsulfanyl]benzimidazoles, e.g., III, as illustrated by the following example. Oxidation of III with cumene hydroperoxide in aqueous EtOAc in the presence of (-)-di-Et D-tartrate, Ti(OPr-iso)4, and DIPEA, gave the (S)-enantiomer of compound II (R8 = NO2) in 95% ee. Substitution of II (R8 = NO2) with sodium ethoxide resulted in the formation of (S)-omeprazole (II; R8 = OMe) with no loss of chirality. The oxidation gives enantiomeric excess of at least 40%, usually above 90%. Compds. of formula I are known to be inhibitors of gastric acid secretion. The process avoids the disadvantage of resolution techniques where material is wasted in the form of the undesired stereoisomer. The process of the invention also avoids the problem of overoxidn. to the corresponding sulfone.

RX(1) OF 3



(step 1)



NOTE: stereoselective, ee = 95%
CON: STAGE(1) room temperature -> 35 deg C; 1 hour, 35 deg C; 35 deg C -> 25 deg C
STAGE(2) 25 deg C
STAGE(3) 15 minutes, 25 deg C; 25 deg C -> 35 deg C; 12 hours, 35 deg C

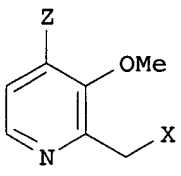
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 22 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:336359 CASREACT
TITLE: process for preparation of pantoprazole via reaction of a mercaptoimidazole with a picoline followed by oxidation and methoxylation
INVENTOR(S): Napoletano, Caterina; Porta, Eleonora; Allegrini, Pietro; Castaldi, Graziano
PATENT ASSIGNEE(S): Dipharma S.P.A., Italy
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

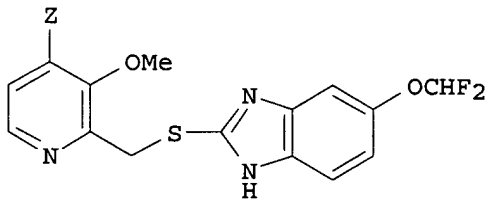
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1518857	A1	20050330	EP 2004-21784	20040914
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2005097302	A	20050414	JP 2004-266846	20040914
US 2005096352	A1	20050505	US 2004-946112	20040922
US 7081534	B2	20060725		
PRIORITY APPLN. INFO.:			IT 2003-MI1813	20030923

OTHER SOURCE(S): MARPAT 142:336359
GI



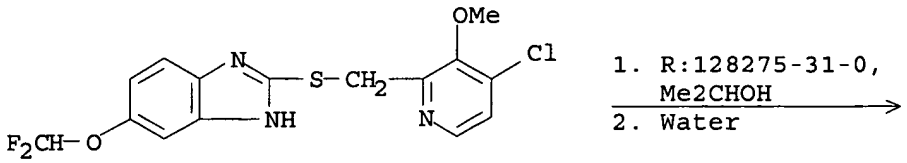
II



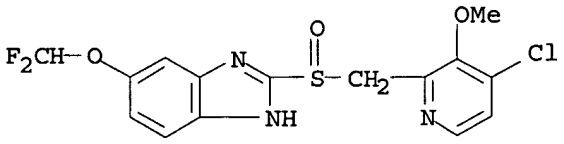
III

AB A process for the preparation of pantoprazole comprises reaction of 5-difluoromethoxy-2-mercaptobenzimidazole (I) with picoline derivs. (II; X, Z = leaving groups) to give pyridinylmethylthiobenzimidazole intermediates (III; Z = leaving group), oxidation thereof with ε-phthalimidoperhexanoic acid, and subsequent methoxylation. Thus, 2-hydroxymethyl-3-methoxy-4-chloropyridine hydrochloride in PhMe was treated dropwise with SOCl2 at 15-25° and kept for ≥1 h. The resulting residue was stirred with NaOMe and I at 15-25° to give 82.8% 5-difluoromethoxy-2-[(4-chloro-3-methoxy-2-pyridinyl)methyl]thio-1H-benzimidazole. The latter in Me2CHOH was treated with ε-phthalimidoperhexanoic acid in Me2CHOH followed by stirring for 5 h to give 84.4% 5-difluoromethoxy-2-[(4-chloro-3-methoxy-2-pyridinyl)methyl]sulfinyl-1H-benzimidazole. This was refluxed with NaOMe in MeOH to give 70.8% pantoprazole sodium salt sesquihydrate.

RX(3) OF 6



(step 1)



84%

CON: STAGE(1) 45 - 90 minutes, 15 - 25 deg C; 5 hours, 25 deg C -> room temperature

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 23 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:219287 CASREACT
TITLE: Process for preparing isomerically pure prodrugs of proton pump inhibitors such as omeprazole and pantoprazole
INVENTOR(S): Garst, Michael E.; Dolby, Lloyd Jay; Esfandiari, Shervin; Mackenzie, Vivian Rose; Avey, Alfred Arthur; Muchmore, David Charles; Cooper, Geoffrey Kenneth; Malone, Thomas C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 44 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005038076	A1	20050217	US 2004-891317	20040713
AU 2004264401	A1	20050224	AU 2004-264401	20040115
CA 2532104	A1	20050224	CA 2004-2532104	20040115
WO 2005016917	A1	20050224	WO 2004-US1154	20040115
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1644352	A1	20060412	EP 2004-702576	20040115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
CN 1823058	A	20060823	CN 2004-80020488	20040115
BR 2004012590	A	20060919	BR 2004-12590	20040115

PRIORITY APPLN. INFO.: US 2003-487340P 20030715
WO 2004-US1154 20040115

OTHER SOURCE(S): MARPAT 142:219287

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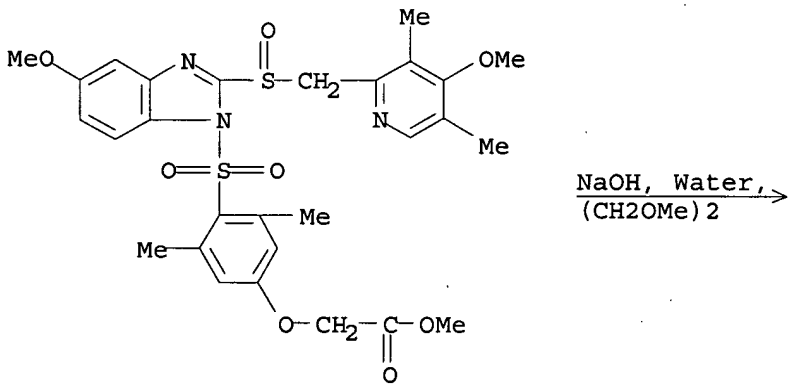
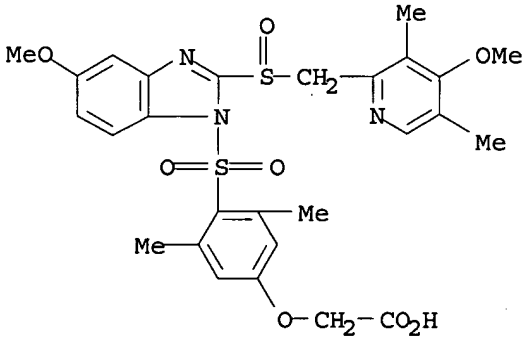
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Syntheses of prodrugs I (R = alkylsulfonyl, arylsulfonyl, substituted arylsulfonyl, heteroarylsulfonyl, substituted heteroarylsulfonyl) of proton pump inhibitors such as omeprazole and pantoprazole are presented. Thus, methyl(3,5-dimethylphenoxy)acetate was added to chlorosulfonic acid to give the corresponding 4-chlorosulfonyl which was alkylated with 4-methoxy-2-nitroaniline. The nitro group of the alkylation product was reduced by treatment with H2 and PtO2, and the resulting amine treated with thiocarbonyl diimidazole to give II. Treatment of II with 4-methoxy-3,5-dimethylpyridinemethanol followed by oxidation with 3-chloroperoxy benzoic acid and treatment with NaOH in H2O/dimethoxyethane gave the desired III.

RX(1) OF 622



RX(1) OF 622



Na

31%

CON: room temperature

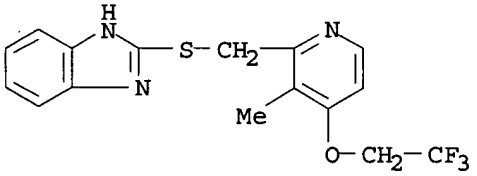
L2 ANSWER 24 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:155946 CASREACT
TITLE: Process of preparing 2-{[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl}sulfinyl-1H-benzimidazole (Lansoprazole)
INVENTOR(S): Piechaczek, Janina; Rytelewska, Jolanta; Glice, Magdalena; Serafin, Jadwiga; Chilmonczyk, Zdzislaw
PATENT ASSIGNEE(S): Instytut Farmaceutyczny, Pol.
SOURCE: Pol., 3 pp.
CODEN: POXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Polish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PL 183815	B1	20020731	PL 1996-314741	19960612

PRIORITY APPLN. INFO.: PL 1996-314741 19960612

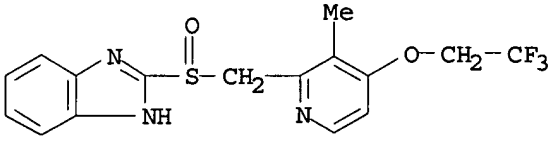
AB The title compound, well known antiulcer agent (no data), was prepared in 92% yield by oxidation of 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]thio]-1H-benzimidazole with MMPP.6H2O in H2O/EtOH.

RX(1) OF 1



(step 1)

1. EtOH
2. R:114915-85-4, Water



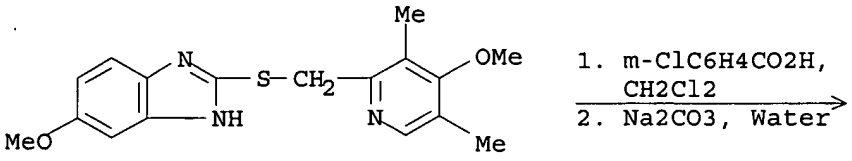
99%

CON: STAGE(1) 20 - 30 deg C
STAGE(2) 5 minutes, 20 - 30 deg C

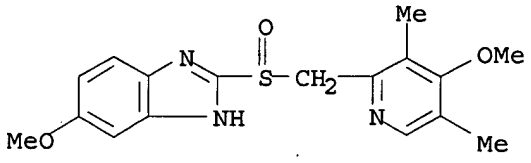
L2 ANSWER 25 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:137027 CASREACT
TITLE: Novel process for omeprazole synthesis
AUTHOR(S): Dai, Li-yan; Wang, Jing-ming; Chen, Ying-qi; Jin, Xu-hu
CORPORATE SOURCE: Institute of Pharmaceutical Engineering, Zhejiang University, Hangzhou, 310027, Peop. Rep. China
SOURCE: Zhejiang Daxue Xuebao, Gongxueban (2004), 38(3), 333-336
CODEN: ZDXGFS; ISSN: 1008-973X
PUBLISHER: Zhejiang Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A process is reported for the production of omeprazole, a proton pump inhibitor, from 2,3,5-trimethylpyridine by oxidation, nitration, methoxylation, rearrangement with methanesulfonic anhydride, condensation with 2-mercapto-5-methoxybenzimidazole and oxidation

RX(6) OF 21



(step 1)



83%

NOTE: 43% overall yield from 2,3,5-trimethyl-Pyridine
CON: STAGE(1) room temperature -> -20 deg C; 1 hour, <-20 deg C; 2 hours, -25 - -20 deg C
STAGE(2) 0.5 hours

L2 ANSWER 26 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:74568 CASREACT
TITLE: A process for preparing 2-[(pyridinyl)methyl]sulfinyl-substituted benzimidazoles and its novel chlorinated derivatives, useful as inhibitors of gastric acid secretion
INVENTOR(S): Lieberman, Anita; Singer, Claude; Raizi, Yuriy
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals Usa, Inc.; Braude, Viviana; Finkelstein, Nina; Chen, Kobi; Pilarsky, Gideon
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

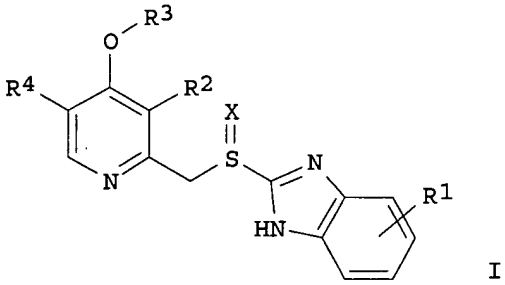
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111029	A2	20041223	WO 2004-US19001	20040610
WO 2004111029	A8	20050421		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2528993	A1	20041223	CA 2004-2528993	20040610
US 2005075370	A1	20050407	US 2004-866261	20040610

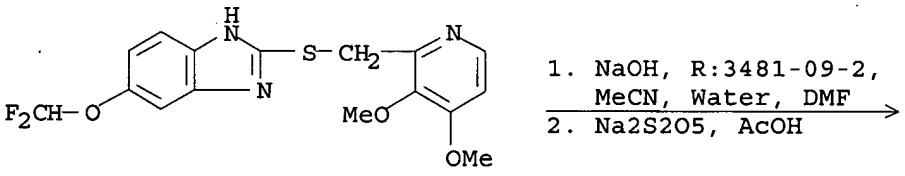
EP 1615913 A2 20060118 EP 2004-755278 20040610
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
CN 1839127 A 20060927 CN 2004-80022239 20040610
PRIORITY APPLN. INFO.: US 2003-477045P 20030610
US 2003-525851P 20031201
WO 2004-US19001 20040610
OTHER SOURCE(S): MARPAT 142:74568
GI



I

AB The invention relates to a preparation of 2-[(pyridinyl)methyl]sulfinyl-substituted benzimidazoles and novel chlorinated derivs. of pantoprazole of formula I [wherein: R1 is H, halogen, alkyl, alkoxy, alkanoyl, or carbethoxy; R2 is H, alkyl, alkoxy, methoxyethoxy, or ethoxyethoxy; R3 is H, alkyl, methoxyethyl, methoxypropyl, or ethoxyethyl; R4 is H, alkyl, fluorinated alkyl, alkoxy, methoxyethoxy, or ethoxyethoxy; X = O], useful as inhibitors of gastric acid secretion (no biol. data). For instance, pantoprazole (I, X = O, R1 = 5-OCHF2, R2 = OMe, R3 = Me, R4 = H) was prepared via S-oxidation of II (X = H2, R1 = 5-OCHF2, R2 = OMe, R3 = Me, R4 = H) by Na2S2O5 with a yield of 98% (the product contains 0.3% of II and free of sulfone within the limit of UV detection).

RX(1) OF 6



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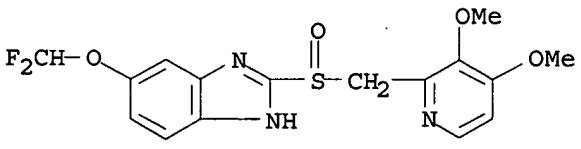


98%

NOTE: optimization study
CON: STAGE(1) room temperature -> -10 deg C; 0.75 hours; 1 hour, room temperature
STAGE(2) pH 8.5

L2 ANSWER 27 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:314329 CASREACT
TITLE: A process for preparation of organic compounds

containing sulfinyl or sulfonyl group via oxidation of thioethers by phthalimidoperhexanoic acid

INVENTOR(S): Allegrini, Pietro; Napoletano, Caterina; Razzetti, Gabriele; Castaldi, Graziano

PATENT ASSIGNEE(S): Dinamite Dipharma S.p.A., Italy; Abbreviated Dipharma S.p.A.

SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

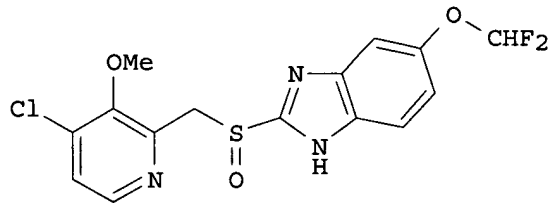
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

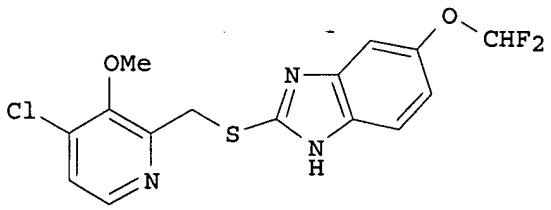
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004192929	A1	20040930	US 2004-801608	20040317
US 6998490	B2	20060214		
EP 1466897	A1	20041013	EP 2004-5420	20040308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
CA 2461833	A1	20040928	CA 2004-2461833	20040325

PRIORITY APPLN. INFO.: IT 2003-MI617 20030328

GI



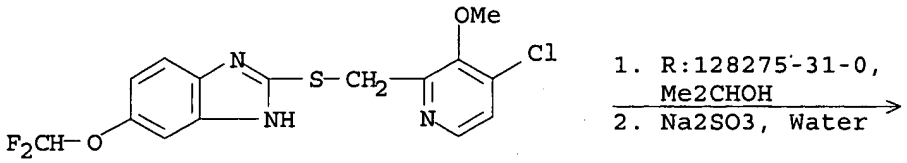
I



II

AB The invention relates to a process of oxidation of thioethers to sulfoxides or sulfones. The oxidation of sulfoxides to sulfones by treatment of thioethers or sulfoxides with an oxidizing amount of phthalimidoperhexanoic acid is useful for the preparation of pharmaceuticals for human or veterinary use. For instance, benzimidazole derivative I was prepared via oxidation of II by phthalimidoperhexanoic acid with a yield of 88.8% (example 1). Phthalimidoperhexanoic acid is a stable, com. available, solid, and cheap oxidizing agent.

RX(1) OF 4



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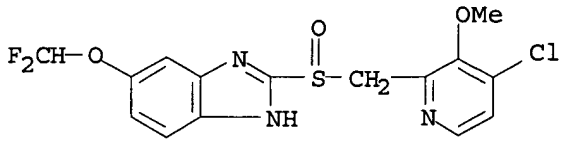


89%

CON: 5 hours

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

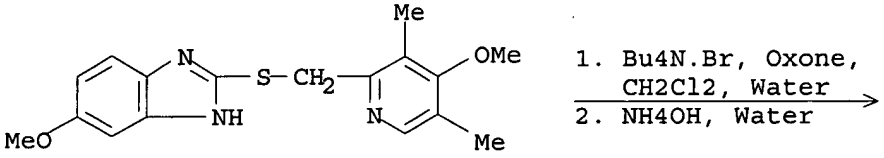
L2 ANSWER 28 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:140456 CASREACT
TITLE: Preparation of sulfoxides by oxidation of sulfides
INVENTOR(S): Jiang, Yunzhen
PATENT ASSIGNEE(S): Institute of Pharmacy, Chinese Academy of Medical Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1377878	A	20021106	CN 2001-110429	20010404

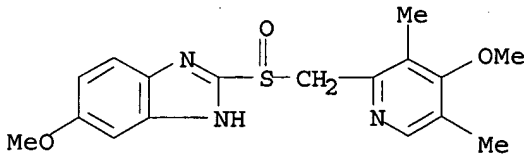
PRIORITY APPLN. INFO.: CN 2001-110429 20010404

AB Sulfoxides are prepared by oxidation of sulfides with oxone in solvent (such as dichloromethane-water, chloroform-water, toluene-water, or benzene-water) in the presence of phase transfer catalyst (such as tetrabutylammonium halide) at (-10)-20°. Omeprazole or other benzimidazolyl sulfoxide derivative were synthesized from 5-methoxy-2-(3,5-dimethyl-4-methoxypyridylmethylthio)-1H-benzimidazole or benzimidazolyl thio ether derivative by the oxidation method, resp.

RX(1) OF 3



(step 1)



79%

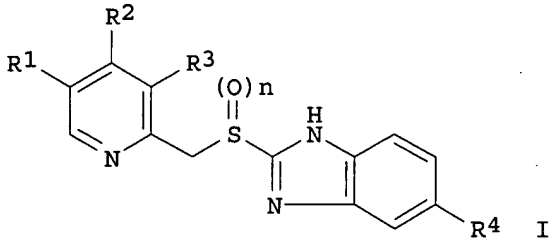
CON: 10 - 15 minutes, -10 deg C

L2 ANSWER 29 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:140445 CASREACT
TITLE: Method for the preparation of pyridinylmethylsulfinylbenzimidazoles which are substantially free of oxidation contaminants for use in pharmaceutical compositions for treatment of gastric ulcers
INVENTOR(S): Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra; Srinivas, Pathi L.
PATENT ASSIGNEE(S): Cipla Limited, India; Wain, Christopher Paul
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004063188	A1	20040729	WO 2004-GB64	20040112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ				
AU 2004203958	A1	20040729	AU 2004-203958	20040112
CA 2513555	A1	20040729	CA 2004-2513555	20040112
EP 1587805	A1	20051026	EP 2004-701384	20040112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006515353	T	20060525	JP 2006-500190	20040112
US 2006205791	A1	20060914	US 2006-542268	20060105

PRIORITY APPLN. INFO.: IN 2003-MU58 20030115
IN 2003-MU193 20030214
WO 2004-GB64 20040112

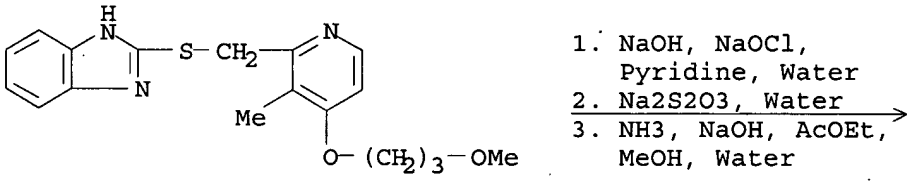
OTHER SOURCE(S): MARPAT 141:140445
GI



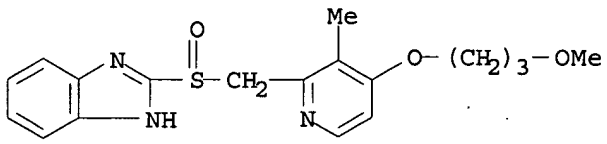
I

AB A process was disclosed for the preparation of sulfinylbenzimidazoles, such as I [R1, R3 = H, Me, alkoxy; R2 = alkoxy; R4 = H, alkoxy; n = 1] free of oxidation contaminants, via oxidation of the corresponding sulfenylbenzimidazoles I (n = 0)using metal hypohalites for therapeutic use in pharmaceutical compns. for the treatment of gastric ulcers. Thus, the sodium salt of rabeprazole I [R1 = H, R2 = O(CH2)3OMe, R3 = H, n = 1] was prepared via oxidation of the corresponding sulfenylbenzimidazole I [R1 = H, R2 = O(CH2)3OMe, R3 = H, n = 0] using a 3.8% sodium hypochlorite solution, sodium hydroxide and pyridine in water.

RX(1) OF 5



(step 1)



Na

CON: STAGE(1) 2 hours, room temperature; 4 hours, 5 - 8 deg C

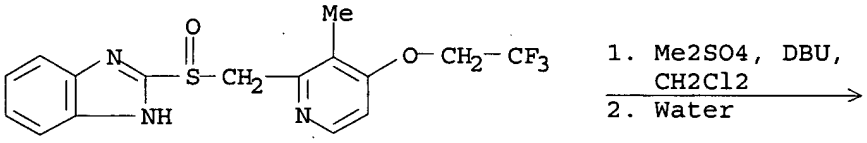
L2 ANSWER 30 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:116452 CASREACT
TITLE: Chemistry of Covalent Inhibition of the Gastric (H+, K+)-ATPase by Proton Pump Inhibitors
AUTHOR(S): Shin, Jai Moo; Cho, Young Moon; Sachs, George
CORPORATE SOURCE: Department of Physiology and Medicine, University of California, Los Angeles, CA, 90073, USA
SOURCE: Journal of the American Chemical Society (2004), 126(25), 7800-7811
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Proton pump inhibitors (PPIs), drugs that are widely used for treatment of

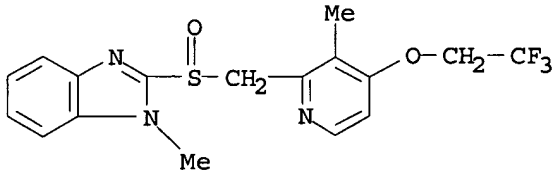
acid related diseases, are either substituted pyridylmethylsulfinyl benzimidazole or imidazopyridine derivs. They are all prodrugs that inhibit the acid-secreting gastric (H+, K+)-ATPase by acid activation to reactive thiophiles that form disulfide bonds with one or more cysteines accessible from the exoplasmic surface of the enzyme. This unique acid-catalysis mechanism had been ascribed to the nucleophilicity of the pyridine ring. However, the data obtained here show that their conversion to the reactive cationic thiophilic sulfenic acid or sulfenamide depends mainly not on pyridine protonation but on a second protonation of the imidazole component that increases the electrophilicity of the C-2 position on the imidazole. This protonation results in reaction of the C-2 with the unprotonated fraction of the pyridine ring to form the reactive derivs. The relevant PPI pKa's were determined by UV spectroscopy of the benzimidazole or imidazopyridine sulfinylmethyl moieties at different medium pH. Synthesis of a relatively acid stable analog, N1-Me lansoprazole, allowed direct determination of both pKa values of this intact PPI

allowing calcn. of the two pKa values for all the PPIs. These values predict their relative acid stability and thus the rate of reaction with cysteines of the active proton pump at the pH of the secreting parietal cell. The PPI accumulates in the secretory canaliculus of the parietal cell due to pyridine protonation then binds to the pump and is activated by the second protonation on the surface of the protein to allow disulfide formation.

RX(12) OF 26



(step 1)



CON: STAGE(1) room temperature
STAGE(2) 30 minutes, room temperature

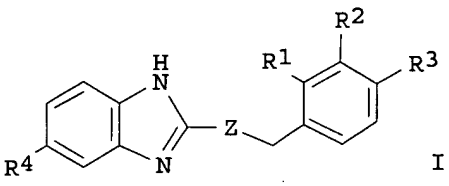
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 31 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:106473 CASREACT
TITLE: Processes for the production of substituted 2-(2-pyridylmethyl) sulfinyl-1H-benzimidazoles
INVENTOR(S): Avrutov, Ilya; Mendelovici, Marioara; Finkelstein, Nina
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S. Ser. No. 66,850.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138466	A1	20040715	US 2003-655645	20030904
US 2003036554	A1	20030220	US 2002-66850	20020204
US 7129358	B2	20061031		
CN 1781918	A	20060607	CN 2005-10086094	20020204
CN 1876647	A	20061213	CN 2006-10081920	20020204
US 2006293363	A1	20061228	US 2006-514964	20060905
PRIORITY APPLN. INFO.:			US 2001-266162P	20010202
			US 2002-66850	20020204
			US 2002-408163P	20020904
			CN 2002-804485	20020204

OTHER SOURCE(S): MARPAT 141:106473

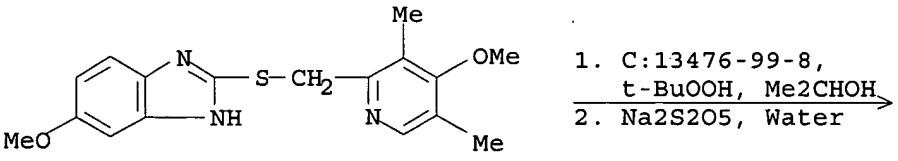
GI



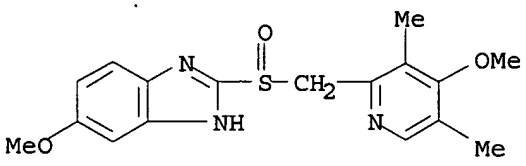
I

AB The present invention discloses improved processes for preparing substituted 2-(2-pyridylmethyl)sulfinyl-1H-benzimidazoles, such as I [R1, R2, R4 = H, alkyl, alkoxy; R3 = H, alkyl; Z = SO], via selective oxidation of a thioether compound II (Z = S), with an oxidizing agent selected from the group consisting of tert-Bu hydroperoxide in the presence of a catalyst, vanadium acetylacetonate, oxone and potassium peroxymonosulfate.

RX(1) OF 5



(step 1)



84%

NOTE: optimization study
CON: STAGE(1) 5 - 7 deg C; 7 deg C -> 22 deg C; 3 hours

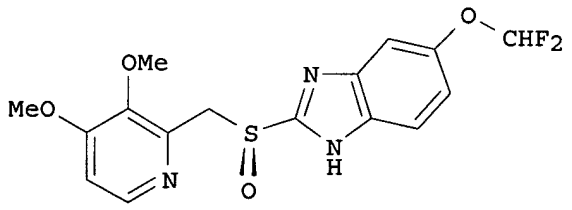
L2 ANSWER 32 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:54346 CASREACT
TITLE: A process for preparing (S)-pantoprazole via stereoselective oxidation of pyridinylmethylsulfinylbenzimidazole derivative in the presence of L-tartaric acid derivative and chiral zirconium or hafnium catalyst
INVENTOR(S): Kohl, Bernhard; Mueller, Bernd; Weingart, Ralf Steffen

10/542,268

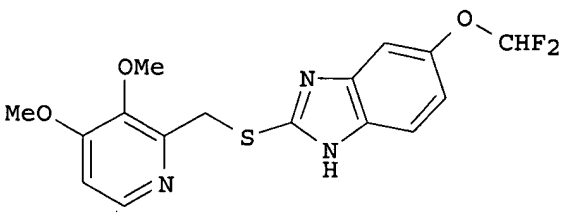
PATENT ASSIGNEE(S): Altana Pharma Ag, Germany
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052881	A2	20040624	WO 2003-EP13604	20031203
WO 2004052881	A3	20041104		
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, EG, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR; HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2507889	A1	20040624	CA 2003-2507889	20031203
AU 2003293749	A1	20040630	AU 2003-293749	20031203
EP 1575941	A2	20050921	EP 2003-789113	20031203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016702	A	20051018	BR 2003-16702	20031203
CN 1717402	A	20060104	CN 2003-80104409	20031203
JP 2006514985	T	20060518	JP 2005-502309	20031203
IN 2005MN00673	A	20051021	IN 2005-MN673	20050627
US 2006167262	A1	20060727	US 2005-536891	20051125
PRIORITY APPLN. INFO.:			EP 2002-27274	20021206
			DE 2003-10340254	20030829
			WO 2003-EP13604	20031203

GI



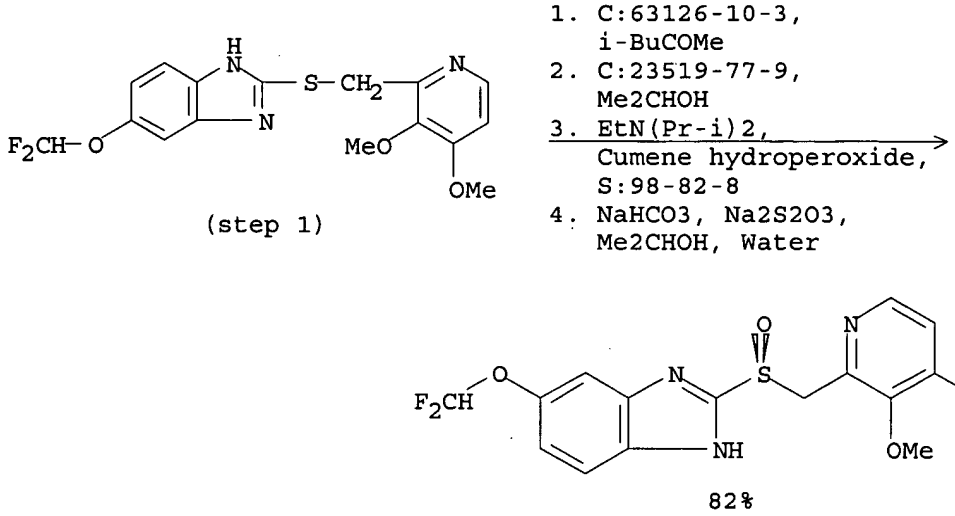
I



II

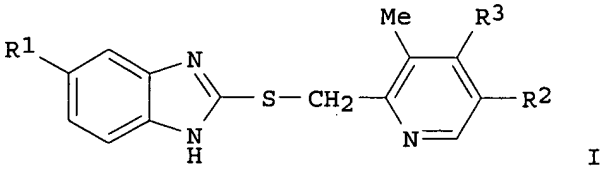
AB The invention relates to a novel process for preparing (S)-pantoprazole (I) via stereoselective oxidation of pyridinylmethylsulfinylbenzimidazole derivative in the presence of L-tartaric acid derivative and chiral zirconium or hafnium catalyst. For instance, the title compound I, useful as proton pump inhibitor, was prepared from thiobenzimidazole derivative II in the presence of L-tartaric acid amide via Zr(IV) isopropoxide catalyzed oxidation by cumene hydroperoxide with a yield of 80% (optical purity was >98%, example 3).

RX(1) OF 1



NOTE: optimization study, optimized on catalyst, stereoselective
CON: STAGE(1) 40 - 45 deg C
STAGE(2) 40 - 45 deg C; 1 hour; 30 deg C
STAGE(3) 20 hours, 30 deg C

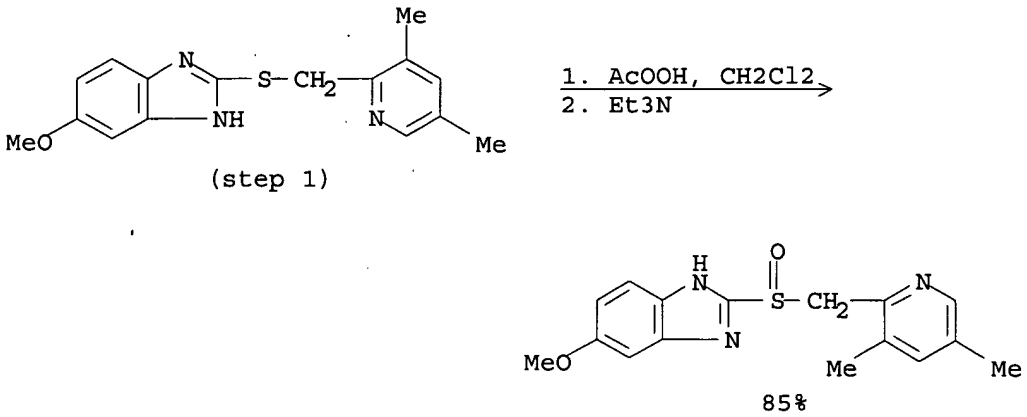
L2 ANSWER 33 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:38563 CASREACT
TITLE: Syntheses of novel pyridine-type benzimidazole derivatives
AUTHOR(S): Dai, Gui-Yuan; Liu, De-Long; Wang, Su-Hui; Liu, Yun
CORPORATE SOURCE: Department of Chemistry, Xuzhou Normal University, Xuzhou, 221116, Peop. Rep. China
SOURCE: Youji Huaxue (2004), 24(3), 315-318
CODEN: YCHHDX; ISSN: 0253-2786
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI



I

AB A series of novel pyridine-type benzimidazole derivs. I (R1 = MeO, Cl, HF2CO, H; R2 = Me, H; R3 = H, Me, OMe) were synthesized and then oxidized to the corresponding sulfoxides in the presence of peracetic acid with excellent yields (76% to 93%). The process was safe and economic for manufacture The structures were established by elemental anal., IR and 1H NMR spectra.

RX(1) OF 30



CON: STAGE(1) 1 hour, -30 - -50 deg C
STAGE(2) 10 minutes, -30 - -50 deg C

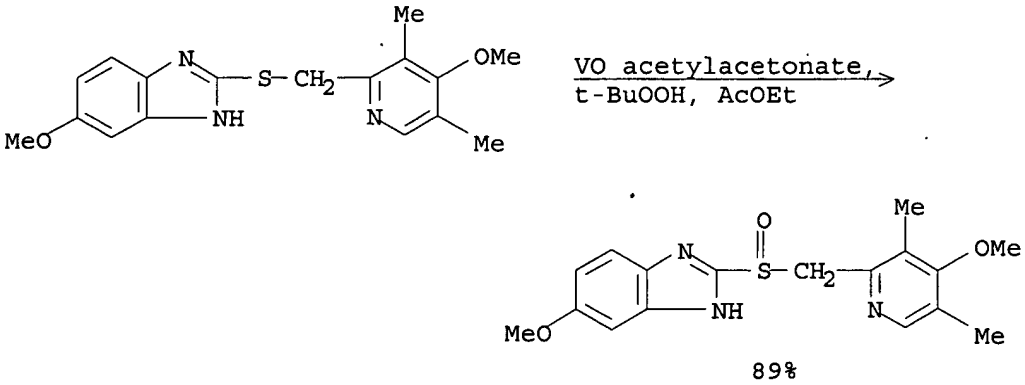
L2 ANSWER 34 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:357338 CASREACT
TITLE: Preparation of sulfinyl-containing drugs by catalytic oxidation of thioether compounds
INVENTOR(S): Yang, Guangzhong
PATENT ASSIGNEE(S): Institute of Pharmacy, Chinese Academy of Medical Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 12 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1381443	A	20021127	CN 2001-109783	20010420

PRIORITY APPLN. INFO.: CN 2001-109783 20010420

AB The thioether compds., such as 5-methoxy-2-(3,5-dimethyl-4-methoxy-2-pyridylmethylthio)-1H-benzimidazole, 2-[3-methyl-4--2-pyridylmethylthio]-1H-benzimidazole, 5-difluoromethoxy-2-(3,4-dimethoxy-2-pyridylmethylthio)-1H-benzimidazole, 2-[4-(3-methoxypropoxy)-3-methyl-2-pyridylmethylthio]-1H-benzimidazole, or (diphenylmethyl)thioacetamide, were oxidized to sulfoxide by using tert-Bu hydroperoxide (tert-Bu hypochlorite, NaClO, H2O2, perbenzoic acid, or 3-chloroperbenzoic acid) in nonprotic solvent (such as dichloromethane, chloroform, CCl4, acetone, Et acetate, etc) in the presence of catalyst (0.5-10%) at 0-25°. The catalyst is titanium tetraisopropoxide, bis(pentane-2,4-dionato)vanadium oxide, bis(pentane-2,4-dionato)copper(II), bis(pentane-2,4-dionato)cobalt(II), tris(pentane-2,4-dionato)iron(III), bis(pentane-2,4-dionato)manganese(II), or tris(pentane-2,4-dionato)chromium(III).

RX(5) OF 8



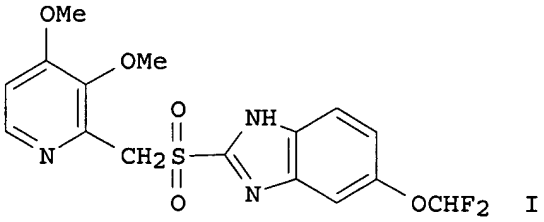
89%

CON: 30 minutes, room temperature

L2 ANSWER 35 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	140:357258 CASREACT
TITLE:	An Improved and Single-Pot Process for the Production of Pantoprazole Substantially Free from Sulfone Impurity
AUTHOR(S):	Mathad, Vijayavitthal T.; Govindan, Shanmugam; Kolla, Naveen Kumar; Maddipatla, Madhavi; Sajja, Eswaraiah; Sundaram, Venkataraman
CORPORATE SOURCE:	Department of Research and Development, Dr. Reddy's Laboratories Ltd., Andhra Pradesh, India
SOURCE:	Organic Process Research & Development (2004), 8(2), 266-270 CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English

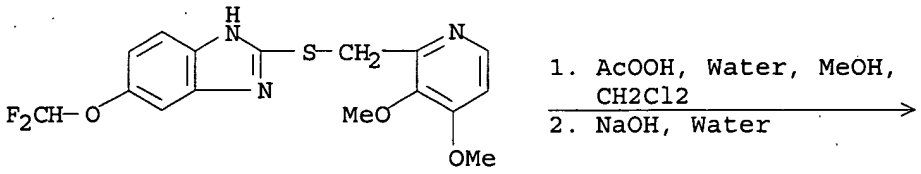
GI



I

AB Pantoprazole, a substituted benzimidazole derivative, is an irreversible proton pump inhibitor, essentially used for the prevention and treatment of gastric acid-related diseases. The process for its preparation generally suffers from the drawback of producing a potential sulfone impurity I. The present work details a report of the journey towards the development of a simple, single-pot process for the production of pantoprazole, substantially free from sulfone impurity I. The detailed study of the different parameters affecting the purity and yield of the compound has been presented.

RX(1) OF 3



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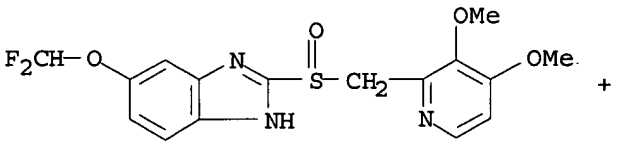
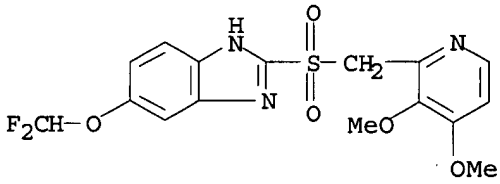


86%

RX(1) OF 3



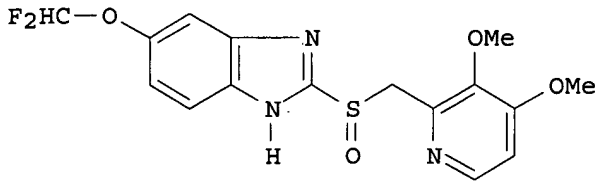
NOTE: safety-toxic reagent, large scale
CON: STAGE(1) 60 - 90 minutes, -10 - -5 deg C; 30 - 45 minutes, -10 - -5 deg C

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

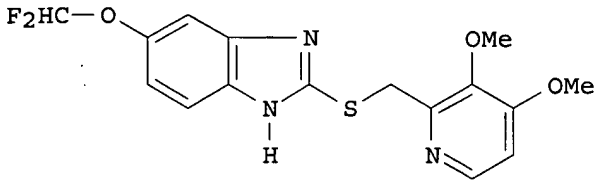
L2 ANSWER 36 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:270848 CASREACT
TITLE: A process for the manufacture of 5-(difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole, i.e., the antiulcer agent pantoprazole, via oxidation of its thio analog
INVENTOR(S): Modi, Prakash Amrut; Motiwala, Jayant Kanaiyalal; Durlabhaji, Chandrakant
PATENT ASSIGNEE(S): Unichem Laboratories Ltd., India
SOURCE: Indian, 12 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 179805	A1	19971213	IN 1994-BO596	19941212
PRIORITY APPLN. INFO.:			IN 1994-BO596	19941212

GI



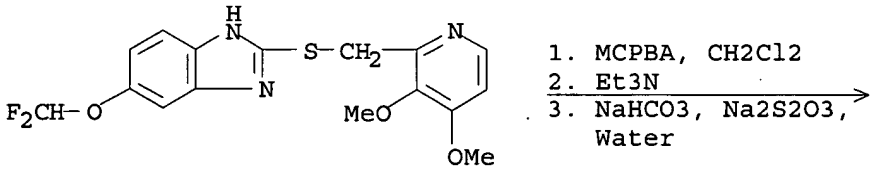
I



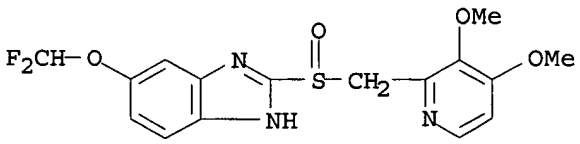
II

AB The invention relates to the preparation of the title compound I (the antiulcer agent pantoprazole) via S-oxidation of thiobenzimidazole derivative II in methylene chloride by m-chloroperbenzoic acid at -50 °C (no yield data). Compound II was prepared from 2-chloromethyl-3,4-dimethoxypyridine and 2-mercapto-5-difluoromethoxy-1H-benzimidazole using NaOH in EtOH at 20-40°.

RX(2) OF 3



(step 1)



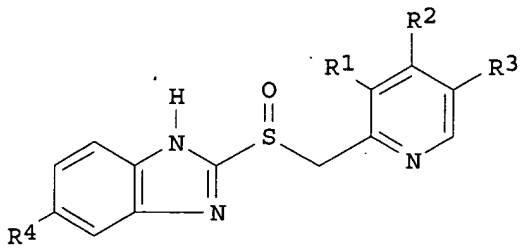
CON: STAGE(1) -50 deg C; 30 minutes, -50 deg C

L2 ANSWER 37 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:146140 CASREACT
TITLE: Preparation of lansoprazole and related compounds
INVENTOR(S): Finkelstein, Nina
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

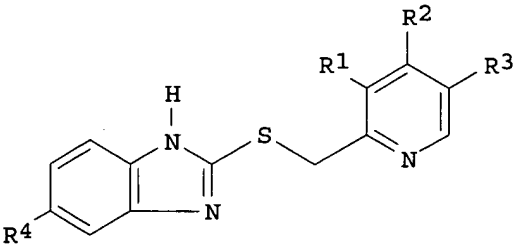
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004011455 A1 20040205 WO 2003-US23588 20030728
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003268034 A1 20040216 AU 2003-268034 20030728
EP 1467987 A1 20041020 EP 2003-748985 20030728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: US 2002-398686P 20020726
WO 2003-US23588 20030728
OTHER SOURCE(S): MARPAT 140:146140

GI



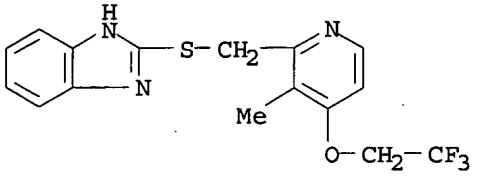
I



II

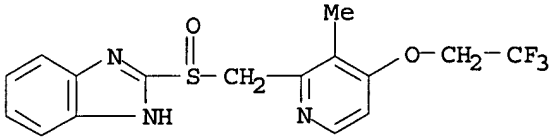
AB The present invention provides a process for preparing lansoprazole (LNP) and related compds. I (R1, R2, R4 = H, alkyl, alkoxy; R3 = H, alkyL) having a high yield and a low level of impurities by oxidation of corresponding sulfides II with tert-Bu hydroperoxide (TBHP), catalyzed by a catalyst vanadium oxytrichloride in an organic solvent selected from the group consisting of a C1-C5 alkanol, decane, nonane, toluene and a mixture of the organic solvent and water, preferably in the presence of a base. Thus, oxidation of 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benimidazole with TBPH in isopropanal in the presence of Et2NH and VOCl3 at 10° for 16 h gave 90% lansoprazole.

RX(1) OF 1



1. VOCl3, t-BuOOH, Et2NH, Me2CHOH
2. Na2SO3, Water

(step 1)



90%

CON: STAGE(1) 16 hours, 10 deg C
STAGE(2) 1 hour, room temperature

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

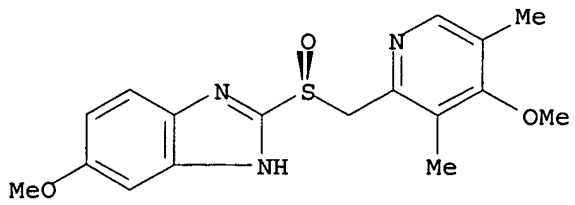
L2 ANSWER 38 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:111413 CASREACT
TITLE: Preparation of Mg salt of [(substituted pyridyl)methyl]sulfinyl-1H-benzimidazole derivatives
INVENTOR(S): Cui, Mingquan; He, Chuanhua; Wang, Xiaoling; Li, Lan; Peng, Jiankun; Qiu, Yu
PATENT ASSIGNEE(S): Chengdu Yaoyou Science and Technology Development Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1367172	A	20020904	CN 2002-113294	20020130

PRIORITY APPLN. INFO.: CN 2002-113294 20020130

AB The Mg salts of [(substituted pyridyl)methyl]sulfinyl-1H-benzimidazole derivs. are prepared by the reaction of [(substituted pyridyl)methyl]sulfinyl-1H-benzimidazole derivs. with soluble Mg salt (such as MgCl2 or Mg(NO3)2) (at a molar ratio of 1:0.45- 0.55) in alkaline solution at pH 9-13.

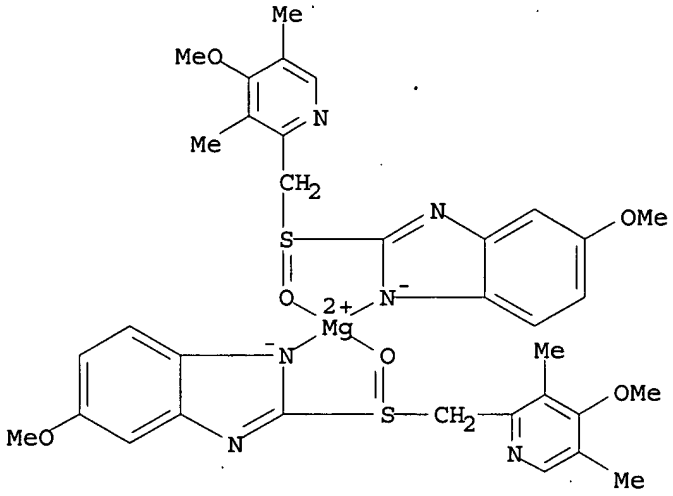
RX(1) OF 5



1. NaOH, Water
2. MgCl2, Water

(step 1)

RX(1) OF 5



CON: STAGE(1) pH 13
STAGE(2) 30 minutes, room temperature, pH 8.1

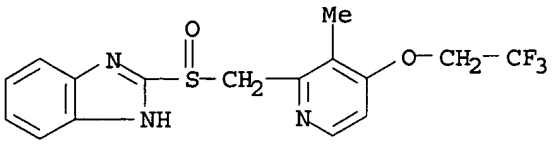
L2 ANSWER 39 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:59642 CASREACT
TITLE: preparation of almost anhydrous lansoprazole from its solvate and/or hydrate
INVENTOR(S): Aihara, Kiyoshi; Hiroshige, Eiko; Yokogoshi, Kiyonori
PATENT ASSIGNEE(S): Permachem Asia, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004002230	A	20040108	JP 2002-160105	20020531

PRIORITY APPLN. INFO.: JP 2002-160105 20020531

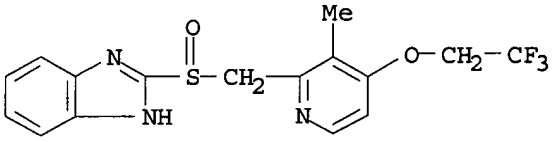
AB Almost anhydrous lansoprazole (I, already know as antiulcer agent) is prepared by dissolving solvate and/or hydrate of I in solvent, crystallizing by aqueous alkali, and drying at low temperature Thus, I hydrate (H2O content 1.5%) was dissolved in DMF, treated with ammonia at pH 9, filtered, and dried at 40° for 12 h to give white I crystals, which contained 0.04% H2O.

RX(1) OF 2



NH3, DMF

H_2O



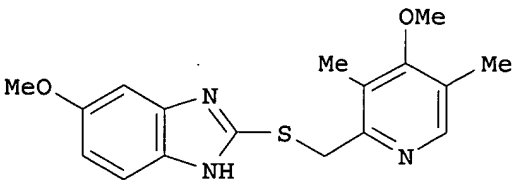
94%

CON: 10 deg C, pH 9

L2 ANSWER 40 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:42173 CASREACT
TITLE: An improved process for the preparation of 5-methoxy-2-(3,5-dimethyl-2-pyridinyl)methyl(sulfinyl)-1-H-benzimidazole (Omeprazole) via sulfide oxidation reaction
INVENTOR(S): Rao, Allavenkata Rama; Deshmukh, Madhusudan Nagorao; Srinivas, Pullela Venkata
PATENT ASSIGNEE(S): Council of Scientific & Industrial Research, India
SOURCE: Indian, 7 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 177319	A1	19961228	IN 1990-DE1277	19901218

PRIORITY APPLN. INFO.: IN 1990-DE1277 19901218
GI

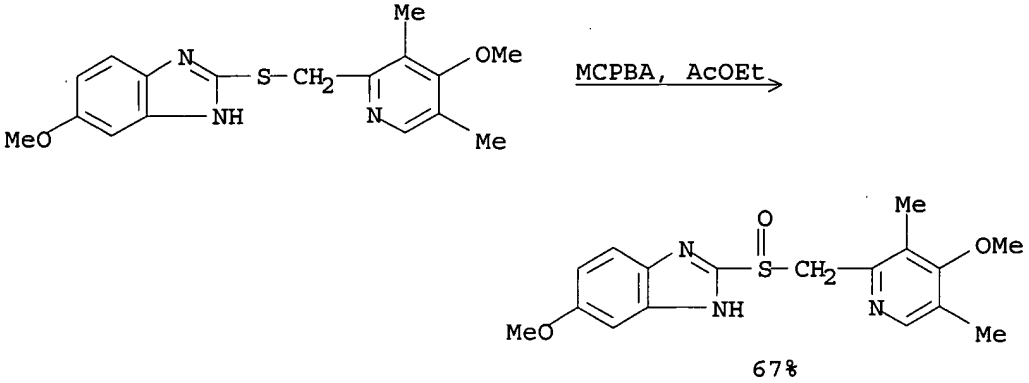


I

AB 5-Methoxy-2([(3,5-dimethyl-4-methoxy-2-pyridinyl)methyl]sulfinyl)-H-benzimidazole (Omeprazole) is prepared by oxidizing the sulfide of the formula I, employing oxidizing agents selected from m-chloroperbenzoic acid, mono-peroxyphthalic acid Mg salts, sodium meta-periodate at -10°C to -12°C, in presence of solvents selected from Et

acetate, water, and acetone.

RX(1) OF 1

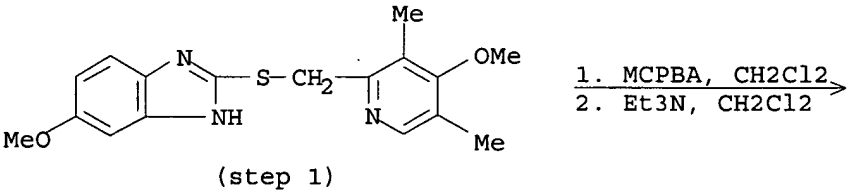


67%

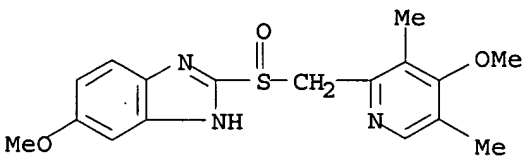
CON: STAGE(1) room temperature -> -12 deg C; 15 - 20 minutes, -10 - -12 deg C; 7 hours, -10 - -12 deg C

L2 ANSWER 41 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 140:28738 CASREACT
TITLE: Synthesis of omeprazole
AUTHOR(S): Liu, Xiulan
CORPORATE SOURCE: Research Department, Shanxi Guardian Pharmaceuticals Co. Ltd, Taiyuan, 030021, Peop. Rep. China
SOURCE: Shanxi Yike Daxue Xuebao (2002), 33(4), 330-332
CODEN: SDXYF5; ISSN: 1007-6611
PUBLISHER: Shanxi Yike Daxue Xuebao Bianjishi
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The title compound was prepared from 5-methoxy-1H-benzimidazole-2-thiol by condensation with 2-(chloromethyl)-4-methoxy-3,5-dimethylpyridine followed by oxidation with m-chloroperoxybenzoic acid. The yield was 84.6%.

RX(3) OF 32



(step 1)



85%

CON: STAGE(1) room temperature -> -10 deg C; 20 minutes, -5 deg C
STAGE(2) 20 minutes, -5 deg C

L2 ANSWER 42 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 139:395935 CASREACT
TITLE: New method for the preparation of the anti-ulcer

compounds omeprazole, lansoprazole and pantoprazole

INVENTOR(S): Correia, Pedro Brito; Romao, Carlos Crispim; Correia, Luis Brito; Pereira, Maria Florbela; Fernandes, Ana Cristina; Borges, Jose Enrique; Tavares, Regina; Costa, Maria Do Ceu; Teixeira, Fatima

PATENT ASSIGNEE(S): Herbex, Produtos Quimicos Sa, Port.; Saragga, Jose Manuel

SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2

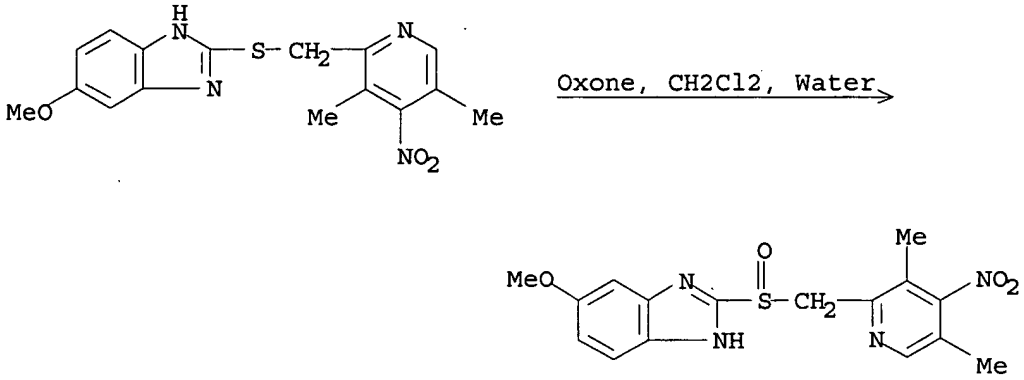
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097606	A1	20031127	WO 2000-IB1057	20000728
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000258410	A1	20031202	AU 2000-258410	20000728
PRIORITY APPLN. INFO.:			WO 2000-IB1057	20000728

OTHER SOURCE(S): MARPAT 139:395935

AB The present invention describes a new process for the intermediate preparation of omeprazole, lansoprazole and pantoprazole , and which involves the formation of pyridines N-oxide using a rhenium compound as a catalyst, followed by nitration of the 4-position with nitric acid fuming in presence of a claycop. The chlorination of the 2-Me group of pyridine was achieved by using the POCl3/Et3N, which allowed the preparation of the derivs. 2-chloromethylpyridines in only one step. These derivs. reacted with the mercaptobenzimidazolic derivs. in presence of ultra-sonic radiation, giving the thioethers. The oxidation of these thioethers was done with several oxidizing agents and the required anti-ulcer compds. were obtained after the substitution of nitro group by the corresponding OR groups. Thus, Omeprazole was prepared by oxidation of 2,3,5-colidine with hydrogen peroxide in presence of methyltrioxorhenium catalyst; nitration; chlorination to form 2-chloromethyl-3,5-dimethyl-4-nitropyridine; reaction with 5-methoxy-2-mercaptobenzimidazole; oxidation; and reaction with sodium methoxide.

RX(5) OF 21



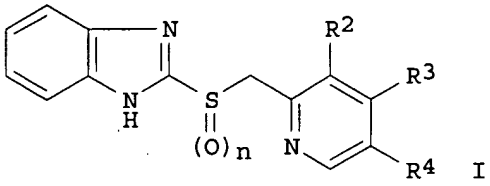
CON: STAGE(1) 0 deg C; 2 hours, 0 - 5 deg C

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 43 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 139:350735 CASREACT
TITLE: Preparation of optically active substituted pyridinylmethylsulfinylbenzimidazoles and salts
INVENTOR(S): Thennati, Rajamannar; Rehani, Rajeev Budhdev; Soni, Rohit Ravikant; Chhabada, Vijay Chhangamal; Patel, Vijaykumar Muljibhai
PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089408	A2	20031030	WO 2003-IN164	20030421
WO 2003089408	A3	20040205		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 194216	A1	20041002	IN 2002-MU299	20020422
IN 2002MU00365	A	20050304	IN 2002-MU365	20020422
AU 2003262375	A1	20031103	AU 2003-262375	20030421
PRIORITY APPLN. INFO.:			IN 2002-MU299	20020422
			IN 2002-MU365	20020422
			WO 2003-IN164	20030421

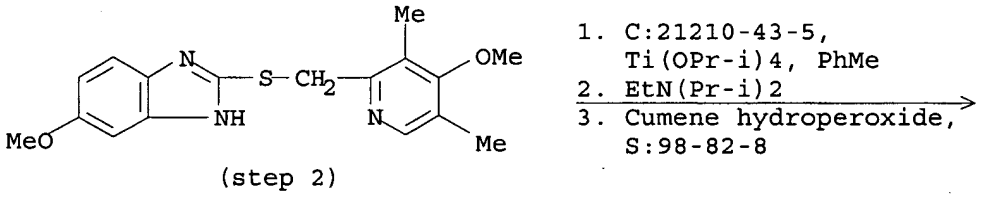
OTHER SOURCE(S): MARPAT 139:350735
GI



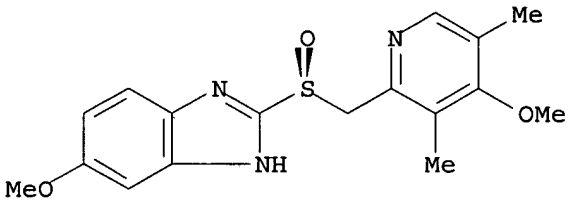
I

AB Optically active enantiomers of the title compds. I [R1-R4 = H, (un)substituted alkyl, alkoxy, aryl, aryloxy; n = 1] are prepared by stereoselective oxidation of I [n = 0] with an oxidizing agent in an organic solvent in the presence of a base and a catalyst comprising titanium or vanadium complexed with a chiral monodentate ligand. The process yields alkali or alkaline earth metal salts of 5-methoxy-2-[(S)-(4-methoxy-3,5-dimethyl-2-pyridinylmethyl)sulfinyl]-1H-benzimidazole substantially free of sulfone impurity, optionally after purification in a ketone or nitrile solvent. Thus, omeprazole sulfide is oxidized with cumene hydroperoxide in presence of EtN(CHMe2)2, Me (S)-(+)-mandelate, and Ti(OCHMe2)4 in PhMe, followed by washing with MeCN to give esomeprazole sodium with >985 ee.

RX(1) OF 1



(step 2)



Na

NOTE: stereoselective
CON: STAGE(1) room temperature -> 40 deg C; 17 hours, 40 deg C; 40 deg C -> 30 deg C
STAGE(2) 25 - 30 deg C; 10 - 15 minutes, 25 - 30 deg C
STAGE(3) 25 - 30 deg C; 2 hours, 25 - 30 deg C

L2 ANSWER 44 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 139:149633 CASREACT
TITLE: A method for eliminating sulfone formation in the synthesis of pyridine-benzimidazole sulfoxides
INVENTOR(S): Uensal, Serafettin
PATENT ASSIGNEE(S): Ulkar Kimya Sanayii Ve Ticaret Anonim Sirketi, Turk.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2

10/542,268

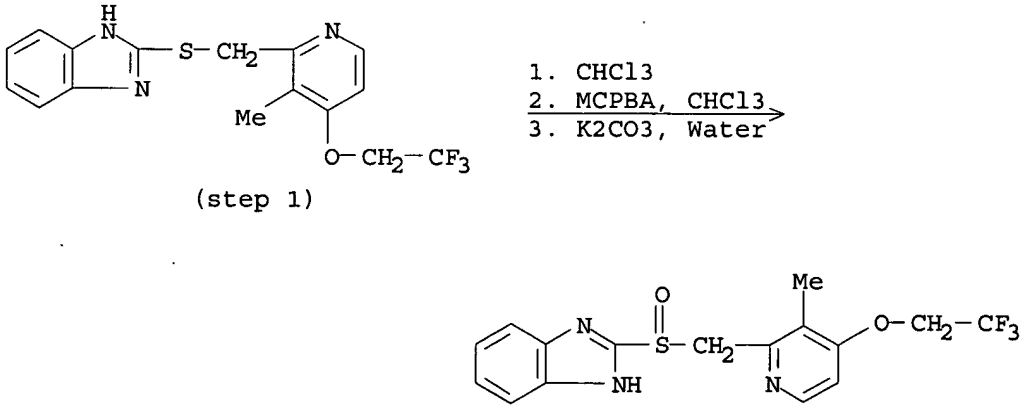
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062223	A1	20030731	WO 2002-TR58	20021001
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1476441	A1	20041117	EP 2002-806580	20021001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
TR 200401671	T1	20050421	TR 2004-1671	20021001
PRIORITY APPLN. INFO.:			TR 2002-186	20020123
			WO 2002-TR58	20021001

OTHER SOURCE(S): MARPAT 139:149633

AB A process is described for the elimination of sulfone analogs in contaminated pyridine-benzimidazole sulfoxide products. The purification process comprises treatment of semi-pure benzimidazole derivs. [e.g., 2-[[3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl]methylsulfinyl]benzimidazole] with solid K2CO3 in alc. medium (e.g., aqueous ethanol) at elevated temps. and by oxidation of the corresponding thioether [e.g., 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl]methyl]thio]benzimidazole] with peracids (e.g., m-chloroperbenzoic acid).

RX(1) OF 1



(step 1)

CON: STAGE(1) room temperature; room temperature -> -20 deg C
STAGE(2) -20 deg C; 8 hours
STAGE(3) 20 - 25 deg C; 20 - 25 deg C, pH 9.9

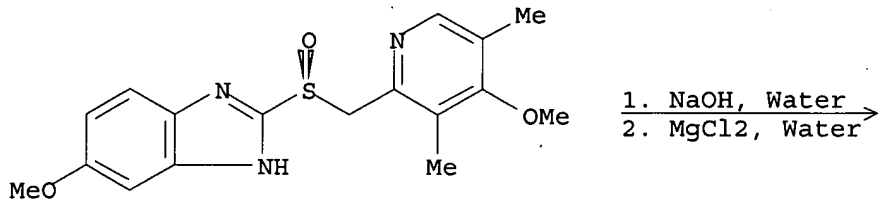
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 45 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 138:264656 CASREACT
TITLE: Research on the synthesis of S-omeprazole magnesium
AUTHOR(S): Cui, Ming-quan; He, Chuan-hua; Chu, Wei; Wang, Xiao-ling; Li, Lan; Peng, Jian-kun
CORPORATE SOURCE: Chengdu Pharmmate Technology Co., Ltd., Chengdu, 610041, Peop. Rep. China
SOURCE: Hecheng Huaxue (2002), 10(3), 193-194
CODEN: HEHUE2; ISSN: 1005-1511
PUBLISHER: Hecheng Huaxue Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

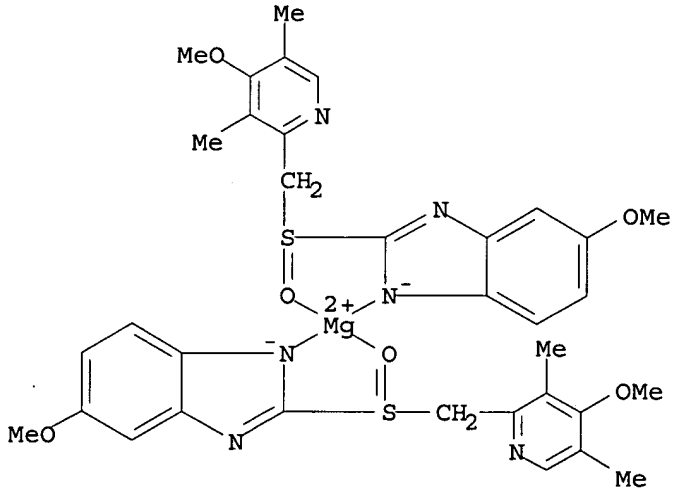
AB A one-pot aqueous synthesis of S-omeprazole magnesium is described. The structure was characterized and identified by IR and 1H NMR.

RX(1) OF 1



(step 1)

RX(1) OF 1



83%

NOTE: optimization on PH
CON: STAGE(1) pH 12
STAGE(2) 40 minutes; 1 hour

L2 ANSWER 46 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 138:205056 CASREACT
TITLE: Preparation of optically pure lansoprazole
INVENTOR(S): Deng, Jingen; Peng, Xiaohua; Cui, Xin; Fu, Fangmin; Zhu, Jin; Chi, Yongxiang; Jiang, Yaozhong
PATENT ASSIGNEE(S): Chengdu Inst. of Organic Chemistry, Chinese Academy of Sciences, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent

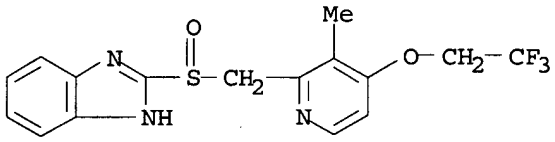
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1329003	A	20020102	CN 2000-113036	20000619
CN 1117747	B	20030813		

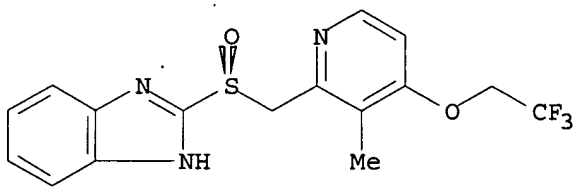
PRIORITY APPLN. INFO.: CN 2000-113036 20000619

AB Lansoprazole is optically resolved by allowing to react with chiral binaphthol (at a molar ratio of 1:2-6) in organic solvent for 12-72 h, standing at 10-30° for 5-48 h, filtering to inclusion compound with one optical configuration, separating lansoprazole and binaphthol from the inclusion compound on chromatog. column to obtain oily or syrup lansoprazole; treating with 1-10% inorg. base solution at 50-120° for 5 min-2 h to pH 10-13 to obtain colorless or light yellow lansoprazole solution; cooling in ice-salt bath for 1-3 h and at -20 to 10° for 5-20 h to obtain white amorphous solid of lansoprazole; and recrystg. to obtain white crystal of lansoprazole.

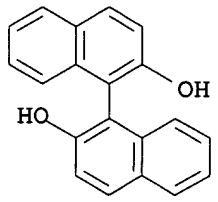
RX(1) OF 10



1,1'-Bi-2-naphthol,
Benzene, Hexane



78%



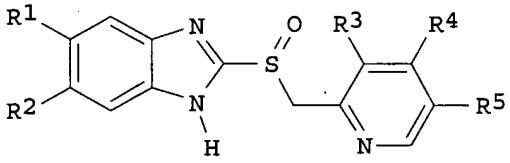
78%

NOTE: alternative prepn. shown
CON: STAGE(1) 60 deg C; 12 hours, 0 deg C

L2 ANSWER 47 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 138:137309 CASREACT
TITLE: Improved process for preparing benzimidazole-type compounds, particularly antiulcer agents such as rabeprazole, by oxidation of sulfide analogs and controlled pH alkaline extraction to remove sulfone impurities
INVENTOR(S): Broeckx, Rudy Laurent Maria; De Smaele, Dirk; Leurs, Stefan Marcel Herman
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003008406 A1 20030130 WO 2002-EP7693 20020709
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2450433 A1 20030130 CA 2002-2450433 20020709
EE 200400052 A 20040415 EE 2004-52 20020709
EP 1409478 A1 20040421 EP 2002-754865 20020709
EP 1409478 B1 20060329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
BR 2002011101 A 20040622 BR 2002-11101 20020709
NZ 530168 A 20040827 NZ 2002-530168 20020709
HU 200400610 A2 20040830 HU 2004-610 20020709
CN 1525970 A 20040901 CN 2002-813961 20020709
JP 2005500333 T 20050106 JP 2003-513965 20020709
AT 321758 T 20060415 AT 2002-754865 20020709
ES 2261703 T3 20061116 ES 2002-2754865 20020709
US 2004209918 A1 20041021 US 2004-483587 20040604
US 6919459 B2 20050719
HK 1069168 A1 20060901 HK 2005-101607 20050225
PRIORITY APPLN. INFO.: EP 2001-202696 20010716
WO 2002-EP7693 20020709
OTHER SOURCE(S): MARPAT 138:137309
GI



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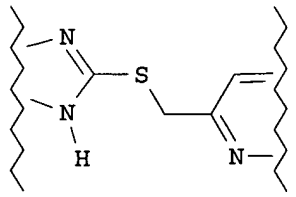
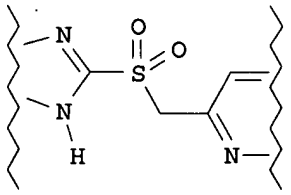
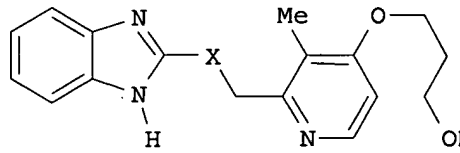


II



III

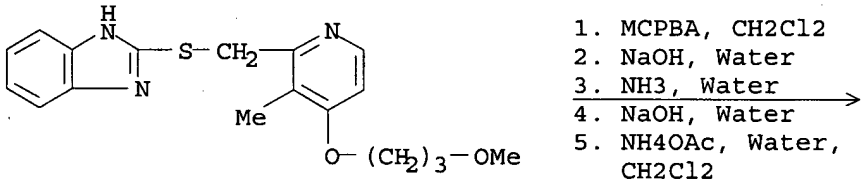


IV

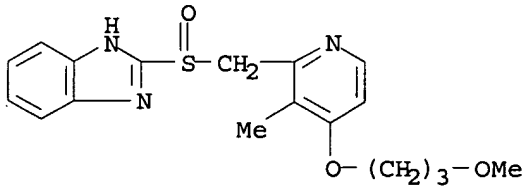
AB The invention relates to an improved process for the preparation of benzimidazole-type proton pump inhibitors, including the antiulcer agents rabeprazole, omeprazole, pantoprazole, lansoprazole, and esomeprazole. The method provides for efficient removal of sulfone impurities in the oxidative production of these sulfoxide drugs. Specifically, the method concerns preparation of sulfoxides I [R1, R2 = H, OMe, OCHF2; R3, R4, R5 = H, Me, OMe, methoxypropoxy, trifluoroethoxy] by oxidation of the corresponding sulfides II, followed by extraction of the sulfone byproducts III with an aqueous alkaline solution at controlled pH. In particular, the reaction mixture is extracted

with an aqueous alkaline solution of pH 9.50-12.00, and the aqueous layer containing III is removed. The organic layer is then extracted with an aqueous alkaline solution of pH 13.0 or higher, and the organic layer containing impurities is removed. Finally, sulfoxides I are isolated from the aqueous layer. By more efficiently removing the sulfone, the method allows for use of higher amts. of oxidizing agent, leading to increased yields. For example, the sulfide precursor of rabeprazole, IV (X = S), was oxidized with 0.88 equiv m-CPBA in CH2Cl2 at -20° over 1.5 h. The reaction mixture was diluted with H2O and the pH adjusted to 10.40 with 10% NaOH, then to 10.85 with aqueous NH3. The aqueous layer (sulfone) was removed, and the organic layer was treated with H2O and the pH raised to 13.0 with 10% NaOH. The organic layer (impurities) was removed, and the aqueous layer (sulfoxide) was treated with CH2Cl2 and adjusted to pH 10.5 with aqueous NH4OAc. The organic layer (sulfoxide) was removed and concentrated, and the residue crystallized from acetone to give rabeprazole, i.e., IV (X = SO) in 57% yield. In contrast, a similar, standard preparation of rabeprazole, using 0.60 equiv m-CPBA and a single extraction at pH 13.0, gave only 44% yield. In both cases, the level of sulfone IV (X = SO2), ≤ 0.8%, was pharmaceutically acceptable. In another experiment, sulfone levels were compared in the prepns. of 3 drugs (new/standard): rabeprazole 0.33%/0.78%, omeprazole 0.26%/0.53%, and lansoprazole 4.1%/11.3% (sic).

RX(1) OF 4



(step 1)



NOTE: controlled pH workup removes sulfone impurity
CON: STAGE(1) 1 hour, -40 deg C; 30 minutes, -40 deg C
STAGE(2) pH 10.40
STAGE(3) pH 11.10
STAGE(4) pH 13.0
STAGE(5) pH 10.44

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

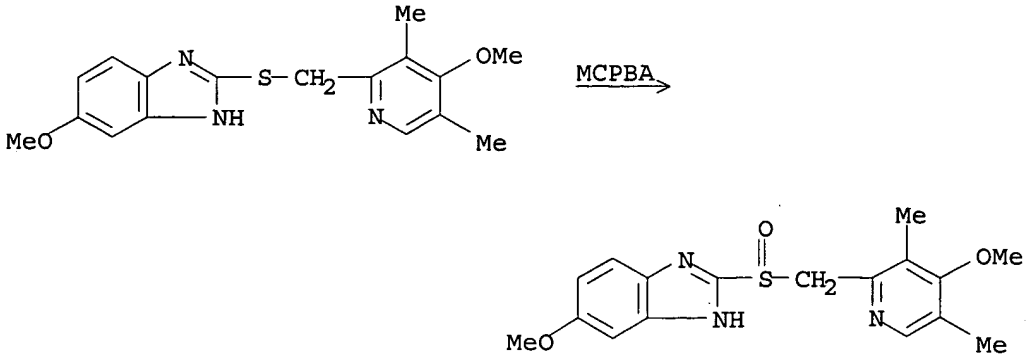
L2 ANSWER 48 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 137:337893 CASREACT
TITLE: Crystallization process for the preparation of a new crystalline form of omeprazole
INVENTOR(S): Hafner, Milae Natasa; Eopar, Anton; Podobnik, Barbara;

Cizerle, Beleie Andreja; Kosak, Alenka; Ornik, Brina; Urleb, Uros
PATENT ASSIGNEE(S): LEK Pharmaceutical and Chemical Company D.D., Slovenia
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085889	A1	20021031	WO 2002-IB1350	20020424
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 20875	A	20021031	SI 2001-111	20010425
CA 2445251	A1	20021031	CA 2002-2445251	20020424
EP 1390360	A1	20040225	EP 2002-764081	20020424
EP 1390360	B1	20061122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200303928	A2	20040301	HU 2003-3928	20020424
BR 2002009103	A	20040713	BR 2002-9103	20020424
JP 2004526786	T	20040902	JP 2002-583416	20020424
CN 1531533	A	20040922	CN 2002-808955	20020424
NZ 528917	A	20060224	NZ 2002-528917	20020424
RU 2286991	C2	20061110	RU 2003-133213	20020424
AT 346063	T	20061215	AT 2002-764081	20020424
ZA 2003007988	A	20041014	ZA 2003-7988	20031014
US 2004122056	A1	20040624	US 2003-475239	20031017
NO 2003004715	A	20031210	NO 2003-4715	20031021
BG 108287	A	20050430	BG 2003-108287	20031024
US 2006079560	A1	20060413	US 2005-248461	20051012
PRIORITY APPLN. INFO.:			SI 2001-111	20010425
			WO 2002-IB1350	20020424
			US 2003-475239	20031017

AB A novel crystalline form of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole (i.e., omeprazole), omeprazole form C (I), a proton pump inhibitor (no data), is prepared via a crystallization process, characterized via X-ray diffraction patterns and FT-IR, and a I-containing pharmaceutical formulation is presented. I form C is prepared by: (a) dissolving crude omeprazole in a solvent or a mixture of solvents in which omeprazole is freely soluble (e.g., methylamine and dichloromethane) ; and (b) precipitating omeprazole form C with a solvent in which omeprazole is poorly soluble (e.g., acetone).

RX(1) OF 1



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 49 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 137:263030 CASREACT
TITLE: Process for the preparation and purification of antiulcer agent lansoprazole
INVENTOR(S): Kim, Wan Joo; Kim, Kyoung Soo; Kim, Myung Hwa; Baek, Yong Gu; Park, Jong Yek; Jang, Jung Min; Choi, Jae Won; Yoo, Yong Sang
PATENT ASSIGNEE(S): Chemtech Research Incorporation, S. Korea; Hansol Chemience Co., Ltd.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002074766	A1	20020926	WO 2002-KR261	20020220
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
KR 2002068592	A	20020828	KR 2001-8677	20010221
EP 1368338	A1	20031210	EP 2002-700866	20020220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004525927	T	20040826	JP 2002-573775	20020220
PRIORITY APPLN. INFO.:			KR 2001-8677	20010221
			WO 2002-KR261	20020220

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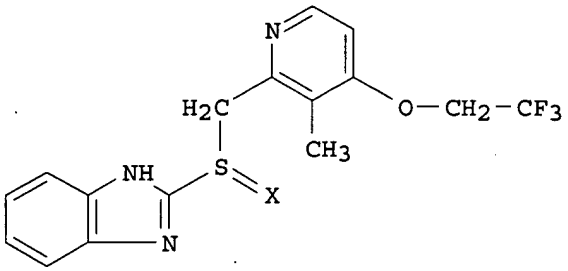

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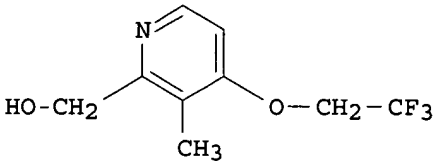
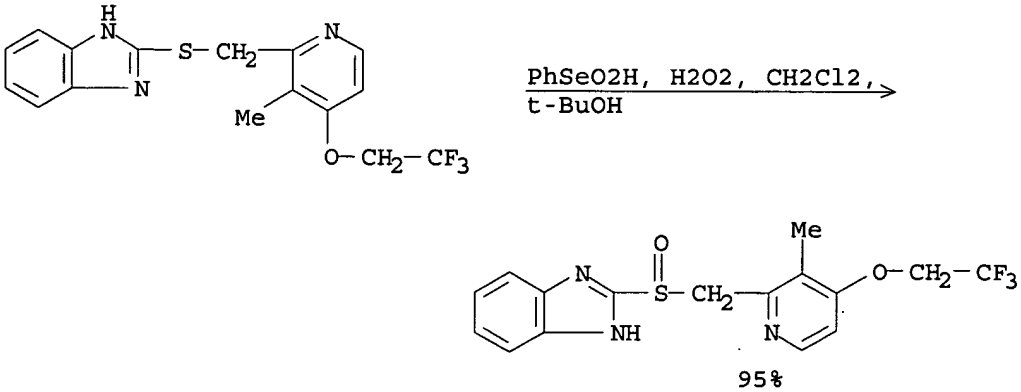


II

AB A process for the preparation of lansoprazole I (X = O) comprising of 2-steps: condensation of pyridine II or its salt with 2-mercaptobenzimidazole in the presence of a halogenating agent and oxidation of sulfide I (X = absent) with hydrogen peroxide in the presence of benzeneseleninic acid as a catalyst is disclosed. For example, to a suspension of sulfide I (X = absent, 4.24 mmol), prepared from pyridine II and 2-mercaptobenzimidazole in 1-step, and benzeneseleninic acid (0.0106 mmol) in CH2Cl2 (30 mL) was added tert-butanol (2 mL) and 35.7% hydrogen peroxide (4.46 mmol) at a temperature below 10 °C. After completion of the reaction, the reaction mixture was cooled to 5 °C, and an aqueous solution of Na2S2O3 (0.4 g/20 mL) added at a temperature below 10 °C. The mixture was vigorously stirred for 30 min., the organic layer separated, washed with water (20 mL), dried over anhydrous Mg2SO4, and concentrated under reduced pressure to afforded after recrystn. lansoprazole in 95% yield. The present process minimizes the production of 2-[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methylsulfinyl-1H-benzimidazole N-oxide byproduct by a simple and economic oxidation method. Lansoprazole is well known as a major component of an anti-ulcer agent having excellent gastric acid secretion inhibiting action and gastric mucous membrane protecting action.

RX(1) OF 11

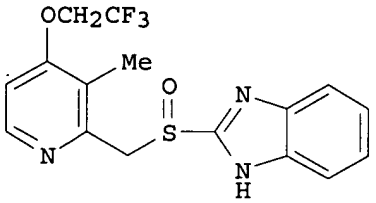


95%

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 50 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 137:262984 CASREACT
TITLE: A new synthetic process of lansoprazole
AUTHOR(S): Ahn, Kwang-Hyun; Kim, Hakwon; Kim, Jeong Ryul; Jeong, Soon Cheol; Kang, Tae Seop; Shin, Hyun Tae; Lim, Geun Jho
CORPORATE SOURCE: College of Environ. and Applied Chem., Yongin City, 449-701, S. Korea
SOURCE: Bulletin of the Korean Chemical Society (2002), 23(4), 626-628
CODEN: BKCSDE; ISSN: 0253-2964
PUBLISHER: Korean Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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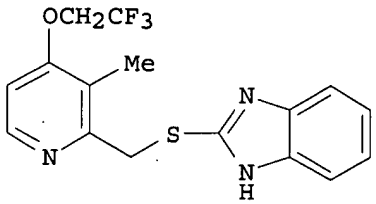
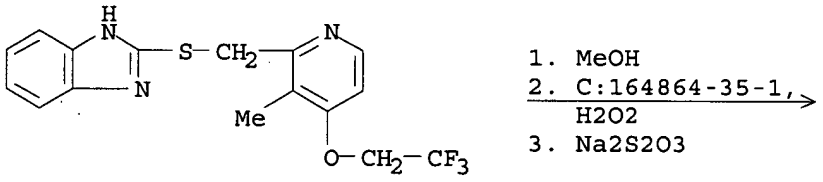


II

AB The proton pump inhibitor, lansoprazole (I) has been prepared in eight steps from 3-methyl-4-nitropyridine 1-oxide in 36% overall yield. The key step in the process is the selective oxidation of sulfide II to I using hydrogen peroxide with a heterogeneous catalyst, LiNbMoO6.

RX(8) OF 36



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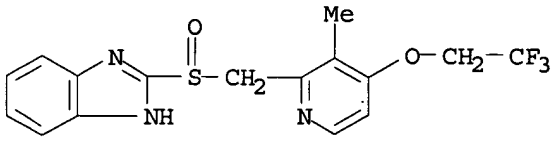

77%

NOTE: key step

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 51 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 137:169521 CASREACT
TITLE: Processes for the production of substituted 2-(2-pyridinylmethyl) sulfinyl-1H-benzimidazoles using tert-butyl hydroperoxide or oxone

10/542,268

INVENTOR(S): Avrutov, Ilya; Mendelovici, Marioara
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceutical USA, Inc.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062786	A1	20020815	WO 2002-US3225	20020204
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
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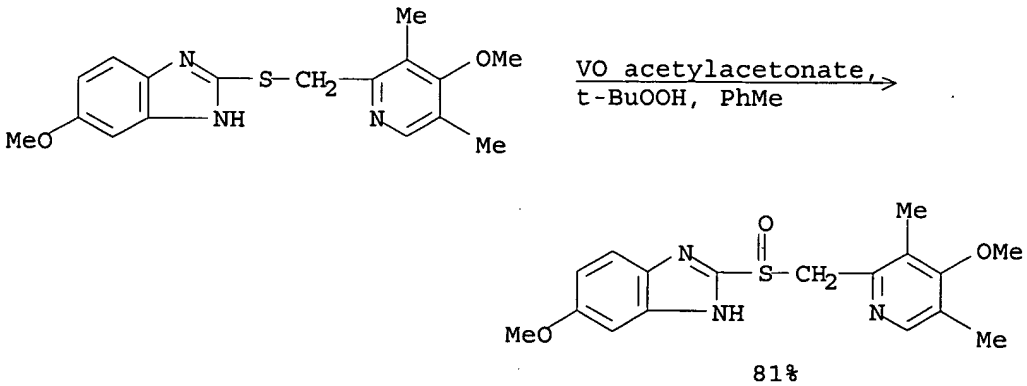
CA 2436467	A1	20020815	CA 2002-2436467	20020204
EP 1363901	A1	20031126	EP 2002-706135	20020204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 200303144	A2	20040301	HU 2003-3144	20020204
CN 1489585	A	20040414	CN 2002-804485	20020204
ZA 2003005652	A	20040722	ZA 2003-5652	20020204
JP 2004524303	T	20040812	JP 2002-563139	20020204
CN 1781918	A	20060607	CN 2005-10086094	20020204
CN 1876647	A	20061213	CN 2006-10081920	20020204
IN 2003MN00726	A	20050429	IN 2003-MN726	20030724
NO 2003003433	A	20030925	NO 2003-3433	20030801
PRIORITY APPLN. INFO.:			US 2001-266162P	20010202
			CN 2002-804485	20020204
			WO 2002-US3225	20020204

OTHER SOURCE(S): MARPAT 137:169521

AB RZR1 (I; Z = SO) [R = (un)substituted 1H-benzimidazol-2-yl; R1 = (un)substituted 2-pyridinyl] were prepared by selective oxidation of I (Z = S) with tert-Bu hydroperoxide or oxone. Oxidation with tert-Bu hydroperoxide were performed in the presence of VO(acac)2, silica bound V2O5 and NaVO3.

RX(1) OF 5



81%

NOTE: optimization study

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

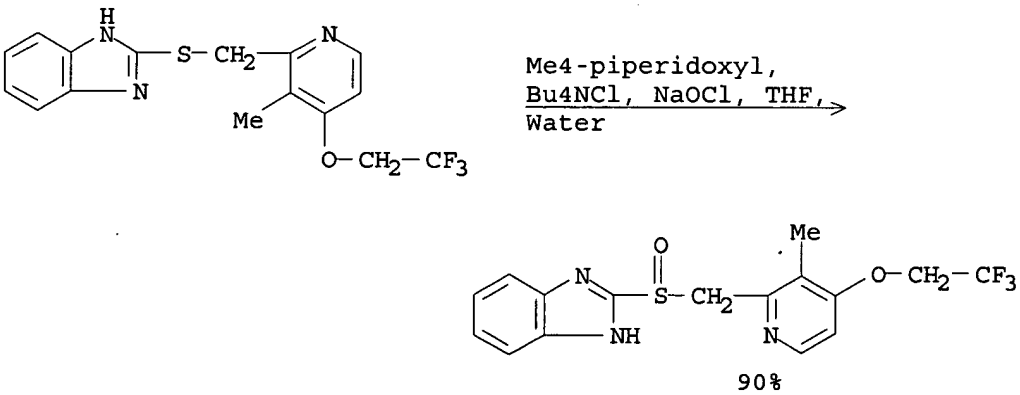
L2 ANSWER 52 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 137:93755 CASREACT
TITLE: Preparation of lansoprazole via coupling of 2-mercaptobenzimidazole with 2-hydroxymethyl-3-methyl-4-(2,2,2-trifluoroethoxy)pyridine followed by radical oxidation.
INVENTOR(S): Moon, Young-Ho; Lee, Kyung-Ik; Lee, Gwan-Sun
PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6423846	B1	20020723	US 2001-967581	20010928

PRIORITY APPLN. INFO.: US 2001-967581 20010928

AB Lansoprazole (I) was prepared by coupling of 2-mercaptobenzimidazole (II) with 2-hydroxymethyl-3-methyl-4-(2,2,2-trifluoroethoxy)pyridine (III) in the presence of a phosphine and a dialkyl azodicarboxylate followed by treatment of the sulfide intermediate with oxidant in a mixture of water and an organic solvent in the presence of an organic free radical and a phase transfer catalyst. Thus, II, III, and Ph3P in THF were treated dropwise with di-Et azodicarboxylate (DEAD) in THF at room temperature, and stirred for 1 h to give 95% 2-[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methylthio-1H-benzimidazole. The latter with tetramethyl-1-piperidinyloxy (TEMPO) in THF, was combined with tetrabutylammonium chloride in water. The resulting mixture was cooled to 0° and aqueous NaOCl was added over 2 h at 0° followed by stirring for 10 min at 0° and then for 10 min at 20° to give 90% I.

RX(1) OF 3



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 53 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:294832 CASREACT
TITLE: A process for the preparation of pantoprazole and intermediates thereof
INVENTOR(S): Palomo Coll, Alberto
PATENT ASSIGNEE(S): Dinamite Dipharma, Italy

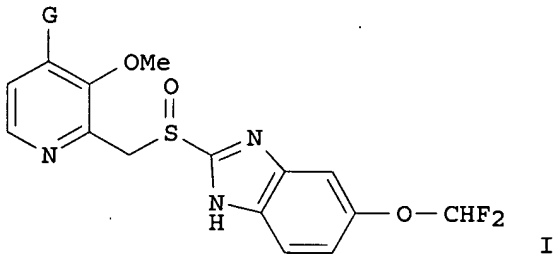
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002028852	A1	20020411	WO 2001-EP11327	20011001
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2185459	A1	20030416	ES 2000-2370	20001002
ES 2185459	B1	20031216		
CA 2424278	A1	20020411	CA 2001-2424278	20011001
AU 2001093856	A5	20020415	AU 2001-93856	20011001
EP 1335913	A1	20030820	EP 2001-974316	20011001
EP 1335913	B1	20040908		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517944	T	20040617	JP 2002-561459	20011001
AT 275561	T	20040915	AT 2001-974316	20011001
ES 2227276	T3	20050401	ES 2001-1974316	20011001
US 2004049044	A1	20040311	US 2003-381978	20030819
US 7060839	B2	20060613		

PRIORITY APPLN. INFO.: ES 2000-2370 20001002
ES 2000-2370 20001002
EP 2001-974316 20011001
WO 2001-EP11327 20011001

OTHER SOURCE(S): MARPAT 136:294832

GI

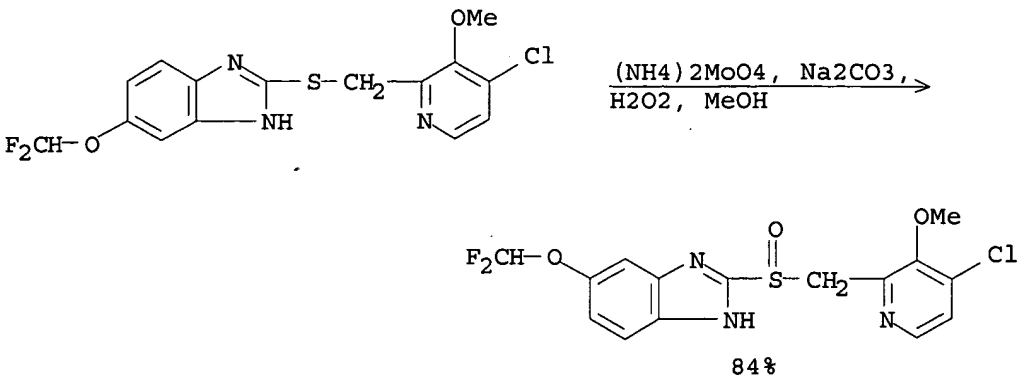


I

AB A process for the preparation of pantoprazole I [G = MeO] is disclosed. 2-Methyl-3-methoxy-4-chloropyridine N-oxide was converted to 2-acetoxy-4-chloro-3-methoxypyridine (Ac2O, DMAP, 65°-70°C) which was deacylated (MeOH, NaOH) and then converted to the corresponding chloromethyl pyridine (CH2Cl2, DMF, SOCl2, 0°C). This intermediate was reacted with 5-difluoromethoxy-2-mercaptobenzimidazole (CH2Cl2, tetramethylguanidine) and the product oxidized (MeOH, [(NH4)2MoO4], H2O2, 0°C, 1-2 days) to the sulfinyl derivative I [G = Cl; II]. Penultimate intermediate II was converted to I by treatment with KOMe in N,N-dimethylacetamide in xx% yield after purification Methoxylation of the chloropyridine moiety is a more selective transformation than prior art in which methylation of a 4-hydroxypyridine intermediate is also prone to

benzimidazole methylation.

RX(4) OF 15



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 54 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:5990 CASREACT
TITLE: Process for producing crystal of optically active 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]benzimidazole
INVENTOR(S): Hashimoto, Hideo; Maruyama, Hideaki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

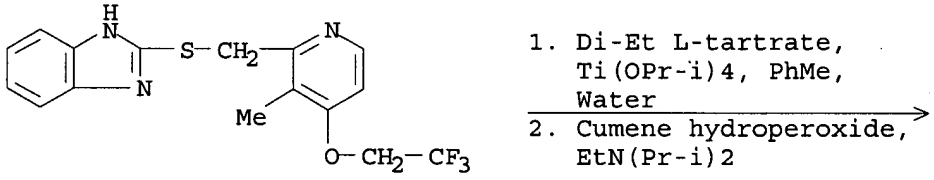
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087874	A1	20011122	WO 2001-JP4014	20010515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 200156732	A	20011126	AU 2001-56732	20010515
JP 2002037783	A	20020206	JP 2001-144635	20010515
JP 3374314	B2	20030204		
CA 2409044	A1	20021114	CA 2001-2409044	20010515
JP 2002338567	A	20021127	JP 2001-145688	20010515
JP 2003055372	A	20030226	JP 2002-229402	20010515
EP 1293507	A1	20030319	EP 2001-930131	20010515
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1437592	A	20030820	CN 2001-811372	20010515
CN 1803137	A	20060719	CN 2005-10131011	20010515
US 2003153766	A1	20030814	US 2002-275334	20021107

US 2007004779 A1 20070104 US 2006-515639 20060905
PRIORITY APPLN. INFO.: JP 2000-141670 20000515
CN 2001-811372 20010515
JP 2001-144635 20010515
WO 2001-JP4014 20010515
US 2002-275334 20021107

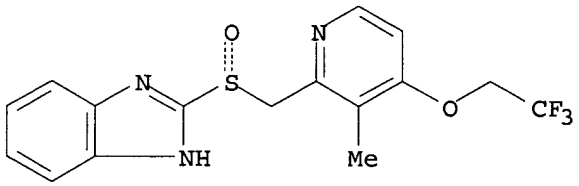
AB Described is a process for producing crystals of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]-sulfinyl]benzimidazole [(R)-I].n'H2O (wherein n' is about 0 to about 0.1) or of a salt thereof, characterized by subjecting a solution or dispersion in an organic solvent of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]benzimidazole .nH2O (wherein n is about 0.1 to about 1.0) to crystallization to crystallize out the target compound During examining various methods of preparing (R)- and (S)-I, it was found that there exist specific crystal forms for (R)- and (S)-I which are different from crystal forms of the sulfone derivative When these isomers are crystallized in these specific crystal forms, surprisingly the sulfone derivative, which is normally difficult to remove, is readily removed to give the desired isomer with very high optical purity. Thereby, this process is a simple process by which an optically active sulfoxide derivative can be efficiently and industrially mass-produced in high yield while attaining an extremely high enantiomer excess. (R)- and (S)-I possess antiulcer, anti-Helicobacter pylori, stomach-acid secretion inhibitory, and mucus membrane-protecting activity and are useful as antiulcer agents (no data). Thus, 0.747 L titanium isopropoxide was added to a mixture of 4.5 kg 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]thio]benzimidazole (1.89% water content), 22 L PhMe, 25 g H2O, 0.958 L (+)-tartaric acid di-Et ester at 50-60° and stirred at the same temperature for 30 min, followed by adding 0.733 L diisopropylethylamine at room temperature and then cumene hydroperoxide at -5° to 5°, and the resulting mixture was stirred at -5° to 5° for 1.5 h and treated with 17 L 30% sodium thiosulfate to decompose the residual cumene hydroperoxide. The organic layer was separated and successively treated with H2O 4.5, heptane 13.5, tert-Bu Me ether 18, and heptane 27 L, and stirred at .apprx.10° for crystallization The precipitated crystals were separated and washed with 4 L tert-Bu Me ether-PhMe (4:1) to give wet crystals of (R)-I containing the sulfone derivative by 0.90% and no sulfide and other isomer with optical purity of 100% ee. A suspension of the latter crystals in 20 L acetone was added dropwise to a mixture of 7 L acetone and 34 L water and stirred at .apprx.10° and the precipitated crystals were separated and washed with a mixture of 4 L acetone and 12 L water to give wet crystals of (R)-I containing no sulfone and sulfide derivative and other isomer with optical purity of 100% ee. The latter wet crystals were dissolved in 45 L EtOAc and 3 L H2O and the organic layer was separated, filtered to remove insol. matter, treated with 0.2 L Et3N, concentrated to .apprx.7 L, and treated with 2.3L MeOH and then with .apprx.12.5% aqueous NH3 (23 L, .apprx.50°) and 22 L tert-Bu Me ether (.apprx.50°). The organic layer was separated while saving the water layer and those in the following procedure, and treated with .apprx.12.5% aqueous NH3, followed by separating the organic layer, and this procedure was repeated one more time. The separated water layers were combined, treated with 22 L EtOAc, adjusted to pH .apprx.8 by adding dropwise AcOH, followed by separating the organic layer and extracting the water layer with 11 L EtOAc. The organic layers were combined, washed with 11 L .apprx.20% aqueous NaCl, treated with 0.2 L Et3N, concentrated under reduced pressure, treated with 5 L acetone, and concentrated under reduced pressure. The concentrate was dissolved in 9 L acetone and the solution was added dropwise to a mixture of 4.5 L acetone and 22.5 L H2O, followed by adding

dropwsie 18 L water to the resulting mixture The resulting mixture was stirred at .apprx.10° and the precipitated crystals were separated and successively washed with a cold 1:3 mixture of acetone and water (3 L) and then 12 L water to give wet crystals of (R)-I containing no sulfone and sulfide derivative and other isomer with optical purity of 100% ee. The latter wet crystals were dissolved in 32 L EtOAc, followed by separating the water layer, and the organic layer was concentrated under reduced pressure to .apprx.14 L, treated with 36 L EtOAc and 270 g activated charcoal, stirred, and filtered to remove the activated charcoal. The filtrate was concentrated under reduced pressure to .apprx.14 L, followed by adding 90 L heptane to the concentrate at .apprx.40° and stirring the resulting mixture at .apprx.40° for 30 min., and the precipitated crystals were separated, washed with a 1:8 mixture of EtOAc and heptane (6 L), and dried to give 3.4 kg (R)-I containing no sulfone and sulfide derivative and other isomer with optical purity of 100% ee, which had specific peaks in powder X-ray diffraction anal.

RX(1) OF 2



(step 1)



NOTE: stereoselective (asym.) oxidn.; 50-60.degree. for 30 min; -5.degree. to 5.degree. for 1.5 h

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 55 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 135:371745 CASREACT
TITLE: Preparation of amorphous forms of omeprazole metal salts having increased stability
INVENTOR(S): Vijayaraghavan, Bakthavathsalan; Sharma, Tarun; Kumar, Naresh
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087831	A2	20011122	WO 2001-IB820	20010511
WO 2001087831	A3	20020328		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

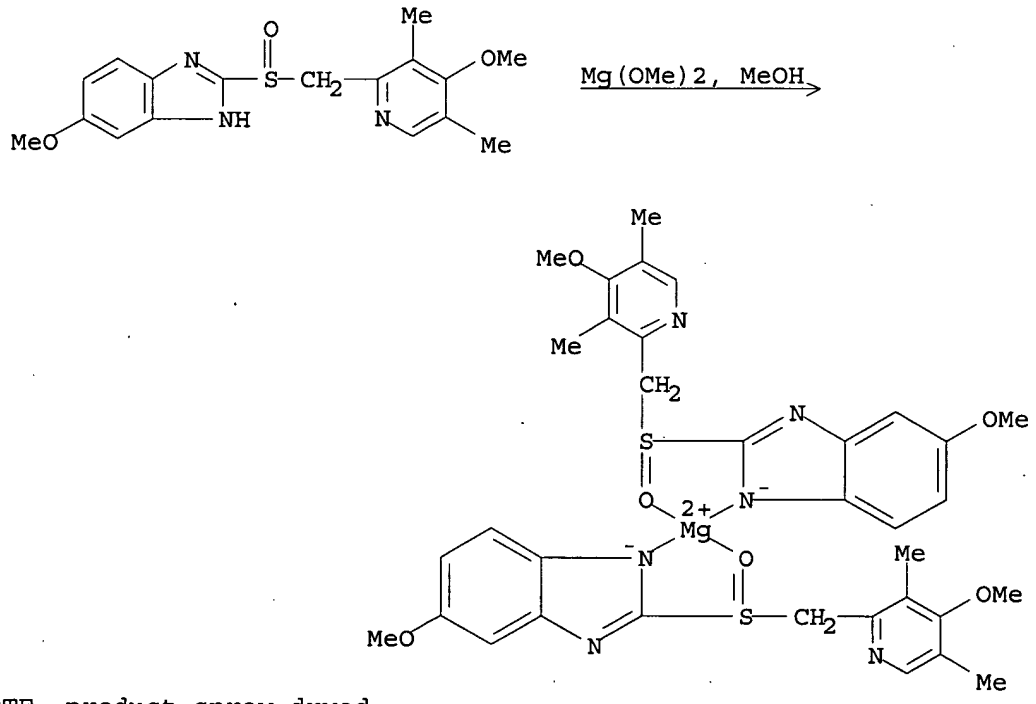
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2409258	A1	20011122	CA 2001-2409258	20010511
AU 2001052486	A5	20011126	AU 2001-52486	20010511
BR 2001010926	A	20040217	BR 2001-10926	20010511
EP 1706397	A2	20061004	EP 2001-925812	20010511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
US 2003212274	A1	20031113	US 2003-276875	20030402
PRIORITY APPLN. INFO.:			IN 2000-DE516	20000515
			WO 2001-IB820	20010511

OTHER SOURCE(S): MARPAT 135:371745

AB Amorphous forms of omeprazole metal salts (e.g., omeprazole magnesium) are prepared by reacting omeprazole with a metal alkoxide A(OR)n (A = Li, Na, K, Mg, Ca, Ti; n = 1 for Group IA metals, 2 for Group IIA metals, and 4 for Ti; e.g., magnesium methoxide) in a nonaq. solvent (e.g., methanol) followed by spray drying of the salt-containing reaction mixture

RX(1) OF 1



NOTE: product spray dryed

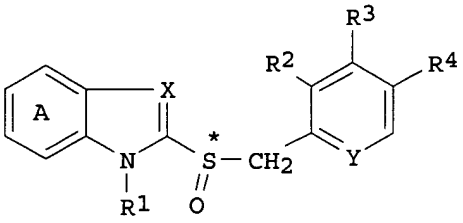
L2 ANSWER 56 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	135:357923 CASREACT
TITLE:	Process for producing optically active pyridylmethylsulfinylbenzimidazole derivatives
INVENTOR(S):	Hashimoto, Hideo; Urai, Tadashi
PATENT ASSIGNEE(S):	Takeda Chemical Industries, Ltd., USA
SOURCE:	PCT Int. Appl., 42 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083473	A1	20011108	WO 2001-JP3613	20010426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 200152595	A	20011112	AU 2001-52595	20010426
CA 2407208	A1	20021022	CA 2001-2407208	20010426
EP 1277752	A1	20030122	EP 2001-925946	20010426
EP 1277752	B1	20061122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 346062	T	20061215	AT 2001-925946	20010426
JP 2002012592	A	20020115	JP 2001-130660	20010427
JP 3543192	B2	20040714		
US 2003171591	A1	20030911	US 2002-276109	20021024
US 6982275	B2	20060103		
PRIORITY APPLN. INFO.:			JP 2000-128760	20000428
			WO 2001-JP3613	20010426

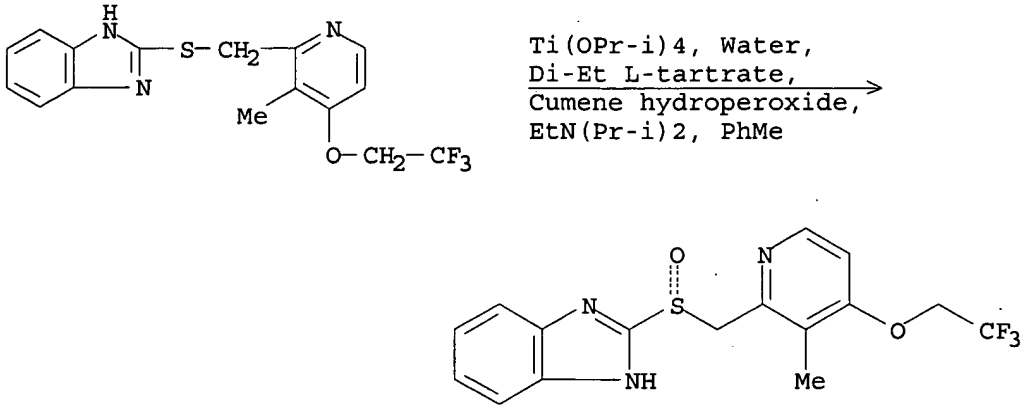
OTHER SOURCE(S): MARPAT 135:357923
GI



I

AB This document discloses a process for producing an optically active isomer of a compound represented by the formula I (wherein ring A represents an optionally substituted benzene ring; R1 represents hydrogen, an optionally substituted hydrocarbon group, acyl, or acyloxy; R2, R3, and R4 each represents hydrogen, optionally substituted alkyl, optionally substituted alkoxy, or optionally substituted amino; X represents nitrogen or CH; Y represents nitrogen or CH; and the asterisk indicates an asym. center) characterized by reacting a pyridylmethylthiobenzimidazole derivative with an excess of an oxidizing agent in the presence of a catalyst for asymmetry induction. Compds. I are antiulcer agents (no data). This process is a simple process by which an optically active sulfoxide derivative can be efficiently and industrially mass-produced in high yield while attaining an extremely high enantiomer excess.

RX(1) OF 2



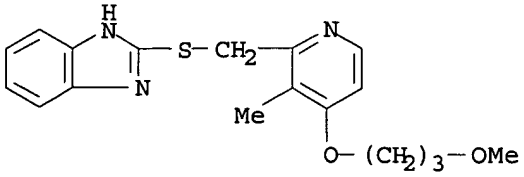
NOTE: stereoselective

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

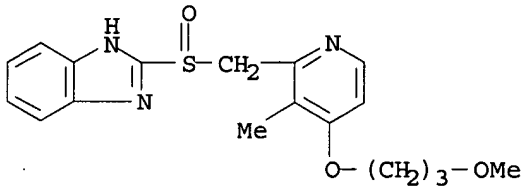
L2 ANSWER 57 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 135:356811 CASREACT
TITLE: Microbial synthesis of a proton pump inhibitor by enantioselective oxidation of a sulfide into its corresponding sulfoxide by Cunninghamella echinulata MK40
AUTHOR(S): Yoshida, Toyokazu; Kito, Mitsuaki; Tsujii, Masahiko; Nagasawa, Toru
CORPORATE SOURCE: Department of Biomolecular Science, Faculty of Engineering, Gifu University, Gifu, 501-1193, Japan
SOURCE: Biotechnology Letters (2001), 23(15), 1217-1222
CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Microbial oxidation of 2-[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylthiobenzimidazole to a useful proton pump inhibitor, sodium 2-[[4-(3-methoxypropoxy)-3-methylpyridin-2-yl] methylsulfinyl]-1H benzimidazole (Rabeprazole), was examined in over 650 microorganisms. Rabeprazole-forming activity was distributed in molds. The mold with the highest activity was identified as Cunninghamella echinulata. Glucose, when added to the reaction mixture, gave the highest accumulation of Rabeprazole (6.9 mM, 2.5 g l-1) with a molar conversion ratio of 92% without the formation of the sulfone form as undesired product and resulted in the exclusive formation of (S) enantiomer (>99% e.e.).

RX(1) OF 1



D-Glucose, Water



92%

NOTE: biotransformation, Cunninghamella echinulata used, chemoselective, stereoselective, buffered soln.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 58 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 135:331424 CASREACT
TITLE: Method for obtaining derivatives of [[(substituted-pyridyl)methyl]thio]benzimidazole, useful as intermediates for omeprazole and related antiulcer agents
INVENTOR(S): Coppi, Laura; Berenguer Maimo, Ramon
PATENT ASSIGNEE(S): Esteve Quimica, S.A., Spain
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079194	A1	20011025	WO 2001-ES143	20010410
WO 2001079194	A9	20030508		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ES 2171116	A1	20020816	ES 2000-989	20000414
ES 2171116	B1	20030801		
AU 2001046551	A5	20011030	AU 2001-46551	20010410
AU 780314	B2	20050317		
CA 2405304	A1	20021007	CA 2001-2405304	20010410
HU 200300583	A2	20030728	HU 2003-583	20010410
JP 2003531144	T	20031021	JP 2001-576794	20010410
EP 1411053	A1	20040421	EP 2001-919463	20010410

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

NZ 521930	A	20040730	NZ 2001-521930	20010410
US 2003036656	A1	20030220	US 2002-204604	20020820
US 6723852	B2	20040420		
NO 2002004858	A	20021206	NO 2002-4858	20021008
PRIORITY APPLN. INFO.:			ES 2000-989	20000414
			WO 2001-ES143	20010410

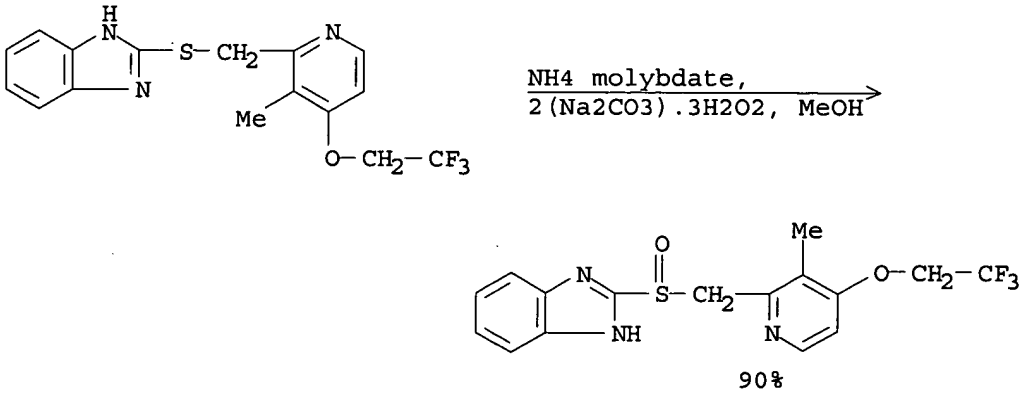
OTHER SOURCE(S): MARPAT 135:331424

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a method for obtaining derivs. of [[(substituted-pyridyl)methyl]thio]benzimidazoles, i.e., I [wherein R1, R3, R4 = H, C1-6 alkyl, alkoxy, or fluoroalkoxy; R2 = NO2, halo, C1-6 alkoxy or haloalkoxy, or O(CH2)nOR8; n = 1-6; R8 = H or C1-6 alkyl]. The method involves the following steps: (a) reaction of a 2-methylpyridine N-oxide II with a carboxylic acid anhydride (R6CO)2O or a sulfonic acid anhydride (R7SO2)2O [R6 = haloalkyl; R7 = (halo)alkyl or (un)substituted aryl]; and (b) reacting the resultant intermediate III [R5 = OCOR6 or OSO2R7] with a corresponding 2-mercaptobenzimidazole. The compds. I are useful as key intermediates for synthesizing corresponding sulfoxides with known antiulcer activity, e.g., omeprazole, lansoprazole, rabeprazole, or pantoprazole. The method offers a reduced number of steps, avoids production of irritating acid chlorides and (chloromethyl)pyridines, and produces fewer residues and byproducts. For instance, reaction of 2,3-dimethyl-4-nitropyridine with (MeSO2)2O in refluxing CHCl3 gave 94% 2-(mesyloxymethyl)-3-methyl-4-nitropyridine methanesulfonate. Reaction of this mesylate with 2-mercapto-1H-benzimidazole and Et3N in CHCl3 at 5-20° gave 82% title compound IV. This intermediate was etherified at the nitro group with CF3CH2OH and K2CO3 (86%), and S-oxidized from the sulfide to the sulfoxide using Na percarbonate and ammonium molybdate catalyst (90%), to give lansoprazole (V).

RX(7) OF 60



NOTE: 10.degree.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 59 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

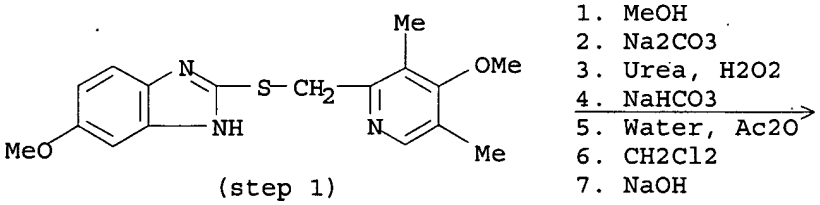
10/542,268

ACCESSION NUMBER: 135:303892 CASREACT
TITLE: Intermediates and an improved process for the preparation of Omeprazole
INVENTOR(S): Prasad, Konakanchi Durga
PATENT ASSIGNEE(S): Natco Pharma Limited, India
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

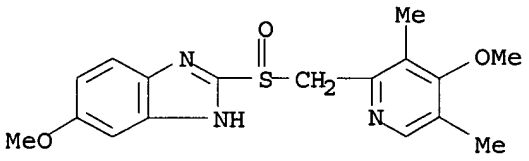
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6303787	B1	20011016	US 1999-427217	19991026
PRIORITY APPLN. INFO.:			IN 1998-MA1129	19980527

AB This invention relates to an improved process for the preparation of Omeprazole starting from 4-nitro-2,3,5-trimethylpyridine N-oxide and through novel intermediates 2-hydroxymethyl-3,5-dimethyl-4-nitropyridine and 2-chloromethyl-3,5-dimethyl-4-nitropyridine. This invention also relates to processes for the preparation of the above said novel intermediates.

RX(5) OF 15



(step 1)



85%

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

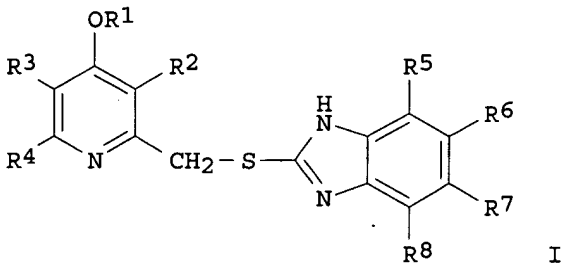
L2 ANSWER 60 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 135:242230 CASREACT
TITLE: Method for oxidizing a thioether group into a sulfoxide group in benzimidazole derivatives
INVENTOR(S): Berenguer Maimo, Ramon; Campon Pardo, Julio; Coppi, Laura
PATENT ASSIGNEE(S): Esteve Quimica, S.A., Spain
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001068594	A1	20010920	WO 2001-ES88	20010308	
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
ES 2163372	A1	20020116	ES 2000-595	20000313	
ES 2163372	B1	20030501			
CA 2402635	A1	20010920	CA 2001-2402635	20010308	
AU 200137452	A	20010924	AU 2001-37452	20010308	
EP 1270555	A1	20030102	EP 2001-909846	20010308	
EP 1270555	B1	20040825			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003527370	T	20030916	JP 2001-567691	20010308	
HU 200301885	A2	20030929	HU 2003-1885	20010308	
NZ 521071	A	20040528	NZ 2001-521071	20010308	
AT 274492	T	20040915	AT 2001-909846	20010308	
PT 1270555	T	20050131	PT 2001-909846	20010308	
ES 2227145	T3	20050401	ES 2001-1909846	20010308	
IN 2002KN01053	A	20050624	IN 2002-KN1053	20020816	
US 2003028030	A1	20030206	US 2002-204506	20020820	
US 6603009	B2	20030805			
NO 2002004239	A	20020905	NO 2002-4239	20020905	
PRIORITY APPLN. INFO.:			ES 2000-595	20000313	
			WO 2001-ES88	20010308	

OTHER SOURCE(S): MARPAT 135:242230

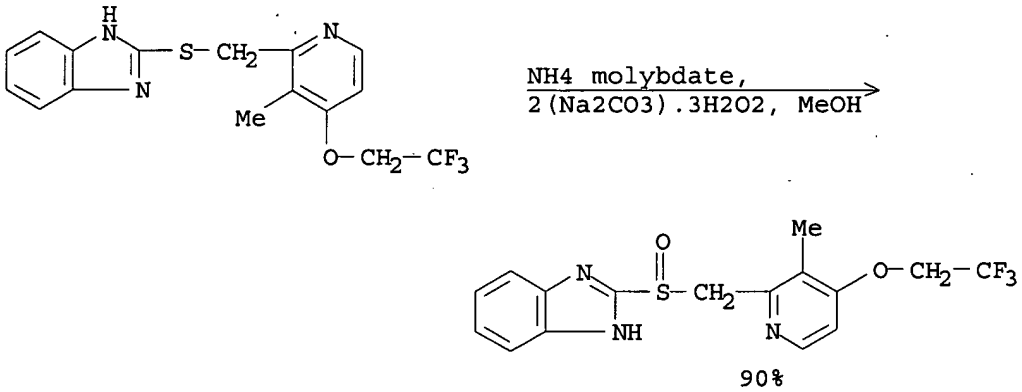
GI



I

AB The invention concerns a method for oxidizing a thioether group into a sulfoxide group using aqueous sodium percarbonate in the presence of a molybdenum salt as catalyst. The method can be used to oxidize the thioether group in compds. I [R1 = C1-C6 alkyl, halo-C1-C6 alkyl or (CH2)nOR9 (n = 1-6; R9 = H, C1-C6 alkyl); R2-R6, R8 = H, C1-C6 alkyl, or C1-C6 alkoxy; R7 = H, C1-C6 alkyl, C1-C6 alkoxy or fluoro-C1-C6 alkoxy] to the corresponding sulfinyl compds. Thus, a treating a methanol solution of 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]thio]-1H-benzimidazole with ammonium molybdate and sodium percarbonate and stirring 15 h at 10° afforded 90% sulfoxide (lansoprazole).

RX(1) OF 1



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

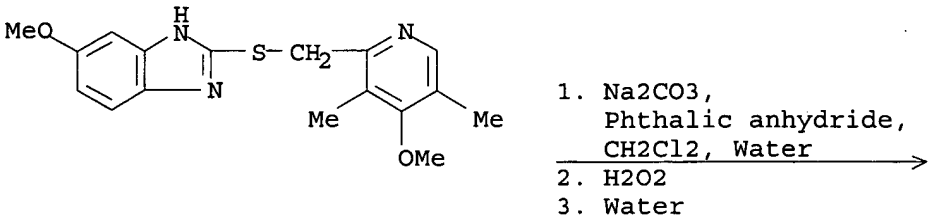
L2 ANSWER 61 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 135:33481 CASREACT
TITLE: Synthetic procedure for 5-methoxy-2-[(4-methoxy-3,5-dimethyl-2-pyridinyl)methylthio]-1H-benzimidazole hydrochloride and its conversion to omeprazole
INVENTOR(S): Singh, Shiva P.; Mukarram, Siddiqui Mohammed Jaweed; Kulkami, Dilip Ganesh; Purohit, Manish
PATENT ASSIGNEE(S): Wockhardt Europe Limited, Ire.
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6245913	B1	20010612	US 1999-343902	19990630

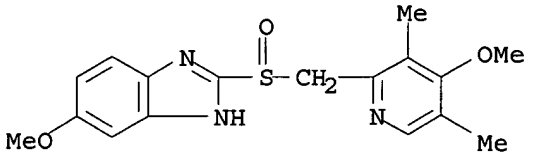
PRIORITY APPLN. INFO.: US 1999-343902 19990630

AB Omeprazole was prepared by (a) oxidizing 3,5-lutidine to its N-oxide with H2O2 and AcOH; (b) reducing excess H2O2 with CH2O; (c) nitrating 3,5-lutidine N-oxide; (d) isolating the 4-nitro derivative; (e)converting the nitro derivative to its di-Me sulfate adduct; (f) treating the di-Me sulfate adduct with aqueous (NH4)2S2O8 to give 2-hydroxymethyl-3,5-dimethyl-4-nitropyridine; (g) converting this compound to the chloromethyl analog; (h) coupling the chloromethyl compound with 5-methoxy-2-mercaptobenzimidazole under phase transfer conditions; (i) nucleophilic substitution of the nitro group by methoxy; (j) oxidation of the sulfide to sulfoxide.

RX(9) OF 45



x HCl
(step 1)



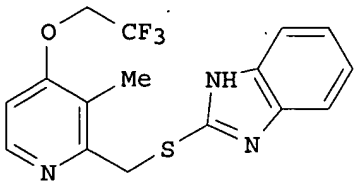
82%

REFERENCE COUNT: 105 THERE ARE 105 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 62 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 134:252340 CASREACT
TITLE: Process for preparing sulfoxide compounds
INVENTOR(S): Choi, Soo Jin; Moon, Seong Cheol; Byun, Young Seok
PATENT ASSIGNEE(S): Daewoong Pharm Co., Ltd., S. Korea; Daewoong Chemical Co., Ltd.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021617	A1	20010329	WO 2000-KR1019	20000907
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
KR 2001028547	A	20010406	KR 1999-40831	19990921
PRIORITY APPLN. INFO.:			KR 1999-40831	19990921

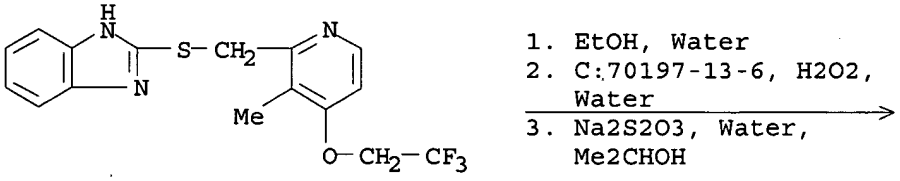
GI



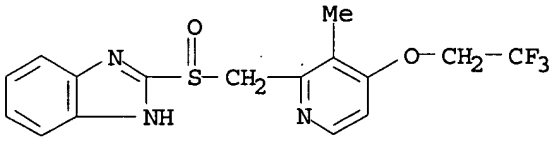
I

AB Oxidation of sulfide compound I with hydrogen peroxide in an ethanol solvent in the presence of methyltrioxorhenium gave the sulfoxide product (94.4%). The process minimizes production of byproducts.

RX(1) OF 1



(step 1)



94%

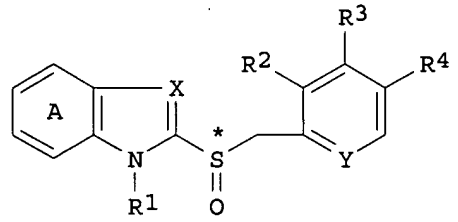
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 63 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 134:193436 CASREACT
TITLE: Process for preparation of optically active sulfoxide derivatives by asymmetric oxidation of sulfide
INVENTOR(S): Kawada, Mitsuru; Yamano, Toru; Taya, Naohiro
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

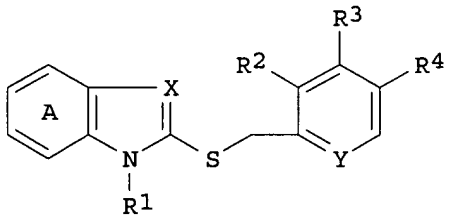
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014366	A1	20010301	WO 2000-JP5682	20000824

W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

JP 2001131172 A 20010515 JP 2000-253771 20000824
PRIORITY APPLN. INFO.: JP 1999-238471 19990825
OTHER SOURCE(S): MARPAT 134:193436
GI



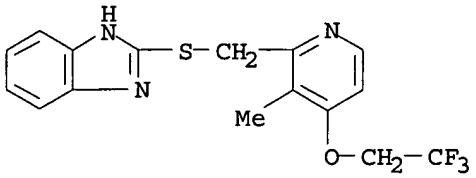
I



II

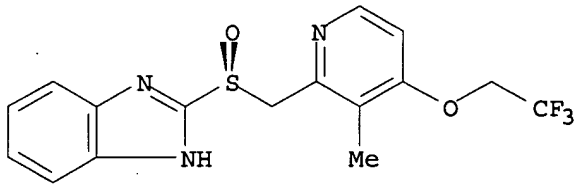
AB Optically active compds. represented by general formula (I; wherein ring A is an optionally substituted benzene ring; R1 is H, optionally substituted aralkyl, acyl, or acyloxy; R2, R3 and R4 are each H, optionally substituted alkyl, optionally substituted alkoxy, or optionally substituted NH2; X and Y are N or CH; and * represents an asym. center) or salts thereof are prepared easily and in an extremely high enantiomeric excess and a high yield by oxidizing compds. represented by general formula (II; ring A, R1-R4 , X, and Y are defined as above) or salts thereof in the presence of both a substance acting as a mol. sieve and an asym. induction catalyst. This process efficiently gives in a large industrial scale, I which possess antiulcer activity (no data). Thus, 2.1 g 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]thio]-1H-benzimidazole containing 105 μL H2O and 2.1 g mol. sieve 4A were mixed, followed by adding 120 μL H2O to make a total water content of 12.5 mmol, and 50 mL PhMe in this order, and the resulting mixture was stirred for 15 min, treated with 2.6 mL (-)-tartaric acid di-Et ester and 1.8 mL titanium(IV) isopropoxide in this order, stirred at 50° for 1 h, and then treated with 1.0 mL i-Pr2NEt and 0.9 mL cumene hydroperoxide in this order and stirred for 3 h to give 77% (S)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1H-benzimidazole (95% ee).

RX(1) OF 2



1. Di-Et D-Tartrate, Ti(OPr-i)4, Water, PhMe
2. EtN(Pr-i)2, Cumene hydroperoxide

(step 1)



77%

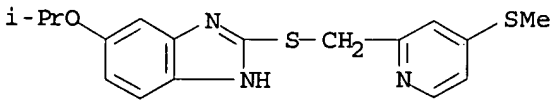
NOTE: mol. sieve 4A, stereoselective

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

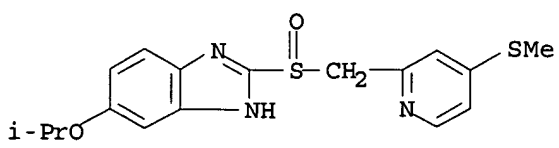
L2 ANSWER 64 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 134:178497 CASREACT
TITLE: Synthesis and characterization of a potent and selective protein tyrosine phosphatase inhibitor, 2-{[4-(methylthio)pyridin-2-yl]methylsulfinyl}benzimidazole
AUTHOR(S): Hamaguchi, T.; Takahashi, A.; Kagamizono, T.; Manaka, A.; Sato, M.; Osada, H.
CORPORATE SOURCE: Medical Research Laboratories, Taisho Pharmaceutical Co., Ltd, Omiya-shi, Saitama, 330-8530, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(23), 2657-2660
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis and biol. activity of a series of 2-{[4-(methylthio)pyridin-2-yl]methylsulfinyl}benzimidazoles is described. These compds. have potent inhibitory effects against the protein tyrosine phosphatase activity of CD45. Enzymic anal. with several phosphatases revealed that 5-isopropyloxy-2-{[4-(methylthio)pyridin-2-yl]methylsulfinyl}benzimidazole had high specificity for CD45 compared with serine/threonine phosphatases, tyrosine phosphatases, and dual phosphatase.

RX(2) OF 6

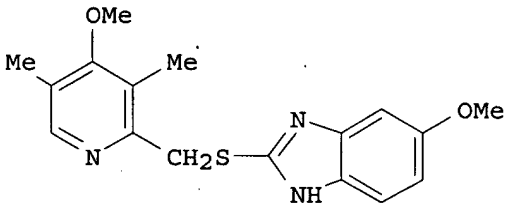


MCPBA, CHCl3



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

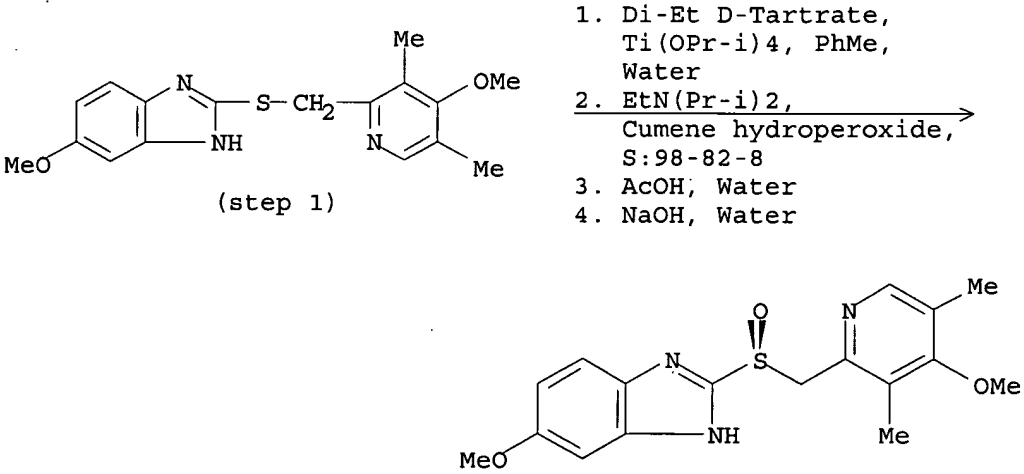
L2 ANSWER 65 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 134:147541 CASREACT
TITLE: Asymmetric synthesis of esomeprazole
AUTHOR(S): Cotton, H.; Elebring, T.; Larsson, M.; Li, L.; Sorensen, H.; von Unge, S.
CORPORATE SOURCE: Process Chemistry, AstraZeneca Process R&D Sodertalje, Soedertaelje, S-151 85, Swed.
SOURCE: Tetrahedron: Asymmetry (2000), 11(18), 3819-3825
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A highly efficient synthesis of esomeprazole - the (S)-enantiomer of omeprazole - via asym. oxidation of prochiral sulfide I is described. The asym. oxidation was achieved by titanium-mediated oxidation with cumene hydroperoxide (CHP) in the presence of (S,S)-diethyl tartrate [(S,S)-DET]. The enantioselectivity was provided by preparing the titanium complex in the presence of I at an elevated temperature and/or during a prolonged preparation time and by performing the oxidation of I in the presence of an amine. An enantioselectivity of >94% ee was obtained using this method.

RX(1) OF 2



(step 1)

NOTE: alternative prepn. gave slightly lower selectivity, stereoselective

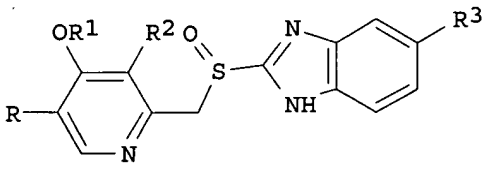
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 66 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 134:86262 CASREACT
TITLE: Process for the production of 2-(2-pyridinylmethylsulfinyl)-1H-benzimidazoles
INVENTOR(S): Cosme Gomez, Antonio; Fau de Casa-Juana Munoz, Miguel; Gelpi Vintro, Jose Maria; Molina Ponce, Andres
PATENT ASSIGNEE(S): Quimica Sintetica, S.A., Spain
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004109	A1	20010118	WO 2000-IB927	20000710
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ES 2166269	A1	20020401	ES 1999-1579	19990714
ES 2166269	B1	20030401		
EG 23175	A	20040630	EG 2000-903	20000712

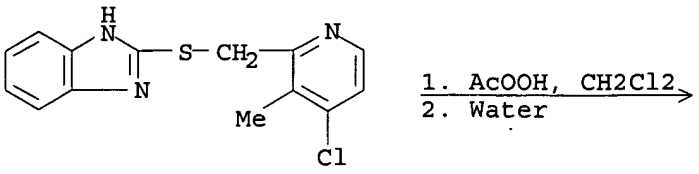
PRIORITY APPLN. INFO.: ES 1999-1579 19990714
OTHER SOURCE(S): MARPAT 134:86262
GI



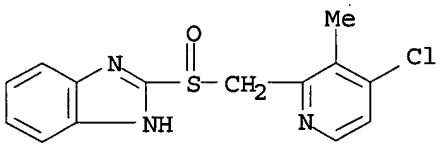
I

AB A procedure for obtaining 2-(2-pyridinylmethylsulfinyl)-1H-benzimidazoles I [R = H, alkyl; R1 = alkyl which may or may not be interrupted by an atom of oxygen; R2 = alkyl, alkoxy; R3 = H, alkoxy] was carried out by the replacement of a halo in position 4 of the pyridine ring by an alkoxide in the presence of a base and within an aprotic polar solvent or by replacement of a nitro group in position 4 of the pyridine ring by an alkoxide radical R1O- is described. E.g., to a solution of 5-methoxy-2-[[(4-nitro-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole (preparation given) in DMSO and methanol is a 30% solution of sodium methoxide in methanol. An 85% yield of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl)-2-pyridinyl]methylsulfinyl]-1H-benzimidazole (Omeprazol) was obtained.

RX(2) OF 16



(step 1)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

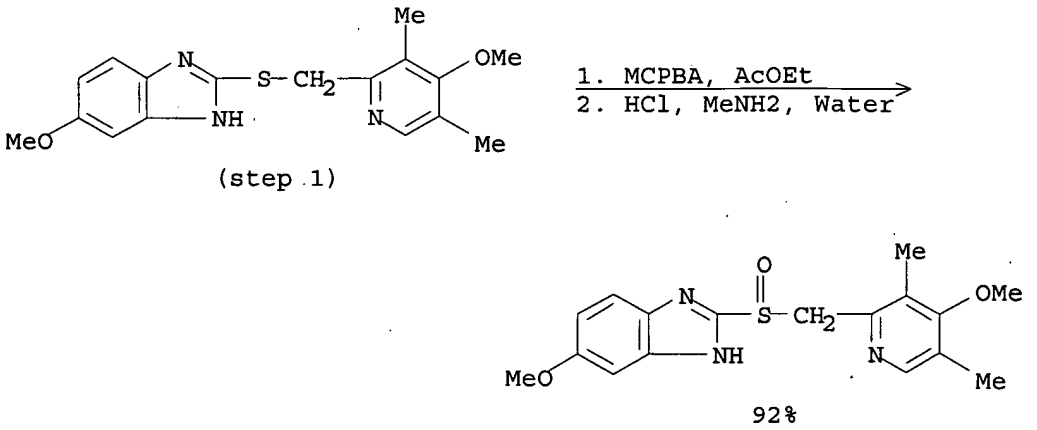
L2 ANSWER 67 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 132:78557 CASREACT
TITLE: Oxidative process of synthesis of 5-methoxy-2-[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfinyl-1H-benzimidazole with precipitative purification
INVENTOR(S): Hafner Milac, Natasa; Jereb, Darja
PATENT ASSIGNEE(S): Lek, Tovarna Farmacevtskih in Kemicnih Izdelkov, D.D., Slovenia
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002876	A1	20000120	WO 1999-SI20	19990712
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SI 20019	A	20000229	SI 1998-196	19980713
AU 9946714	A	20000201	AU 1999-46714	19990712
EP 1095037	A1	20010502	EP 1999-930107	19990712
EP 1095037	B1	20020417		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 200102523	A2	20011128	HU 2001-2523	19990712
NZ 509000	A	20011221	NZ 1999-509000	19990712
AT 216382	T	20020515	AT 1999-930107	19990712
RU 2197486	C2	20030127	RU 2001-103900	19990712
CZ 293653	B6	20040616	CZ 2001-123	19990712
US 6268502	B1	20010731	US 2000-463651	20000830
US 2002007069	A1	20020117	US 2001-919068	20010730
PRIORITY APPLN. INFO.:			SI 1998-196	19980713
			WO 1999-SI20	19990712

US 2000-463651 20000830

AB 5-Methoxy-2-[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfinyl-1H-benzimidazole (omeprazole) is readily prepared by the liquid-phase oxidation of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]thio]benzimidazole with 3-chloroperoxybenzoic acid in Et acetate, where omeprazole is poorly soluble, at -10° to +5°. The crude omeprazole is then purified by dissoln. into an aqueous methylamine solution, followed by precipitation under the addition of hydrochloric acid.

RX(1) OF 1



(step 1)

92%

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 68 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 131:286456 CASREACT

TITLE: Selective oxidation of 5-methoxy-2-[(3,5-dimethyl-4-methoxy-2-pyridyl)methylthio]-1-H-benzimidazole to (RS-5-methoxy-2-[[(3,5-dimethyl-4-methoxy-2-pyridyl)methyl]sulfinyl]-1-H-benzimidazole (omeprazole)

AUTHOR(S): Oelschlager, H.; Seeling, A.; Seeling, B.; Westesen, K.; Bunjes, H.

CORPORATE SOURCE: Institut fur Pharmazie der Friedrich-Schiller-Universitat, Jena, Germany

SOURCE: Pharmazie (1999), 54(10), 734-737
CODEN: PHARAT; ISSN: 0031-7144

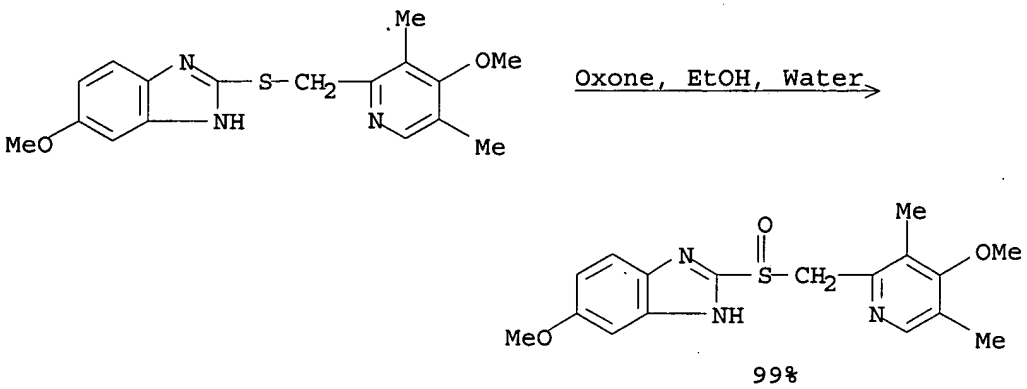
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag

DOCUMENT TYPE: Journal

LANGUAGE: German

AB 5-Methoxy-2-[(3,5-dimethyl-4-methoxy-2-pyridyl)methylthio]-1-H-benzimidazole was oxidized with Oxone in diluted EtOH at -5° furnishing omeprazole with an excellent yield. Addnl., decomposition kinetics of omeprazole in aqueous EtOH are presented.

RX(1) OF 1



99%

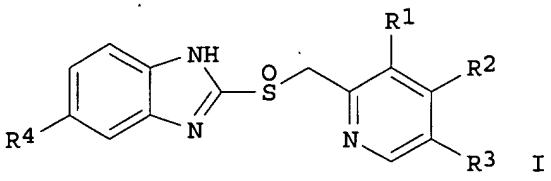
NOTE: method is more environmentally-friendly than other methods

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 69 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 131:228722 CASREACT
TITLE: Preparation of 2-(2-pyridylmethylsulfinyl)-1H-benzimidazoles by perborate oxidation of the corresponding 2-(2-pyridylmethylthio)-1H-benzimidazoles.
INVENTOR(S): Brennan, James Patrick; Turner, Andrew Timothy
PATENT ASSIGNEE(S): Knoll Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947514	A1	19990923	WO 1999-EP1574	19990311
W: AL, AU, BG, BR, BY, CA, CN, CZ, GE, HR, HU, ID, IL, IN, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, AM, AZ, KG, MD, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2323422	A1	19990923	CA 1999-2323422	19990311
AU 9934106	A	19991011	AU 1999-34106	19990311
BR 9908835	A	20001121	BR 1999-8835	19990311
TR 200002670	T2	20001121	TR 2000-20000267	19990311
EP 1071678	A1	20010131	EP 1999-915569	19990311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI				
HU 200101230	A2	20011028	HU 2001-1230	19990311
JP 2002506862	T	20020305	JP 2000-536710	19990311
TW 473476	B	20020121	TW 1999-88104130	19990317
NO 2000004580	A	20000914	NO 2000-4580	20000914
PRIORITY APPLN. INFO.:			GB 1998-5558	19980317
			WO 1999-EP1574	19990311

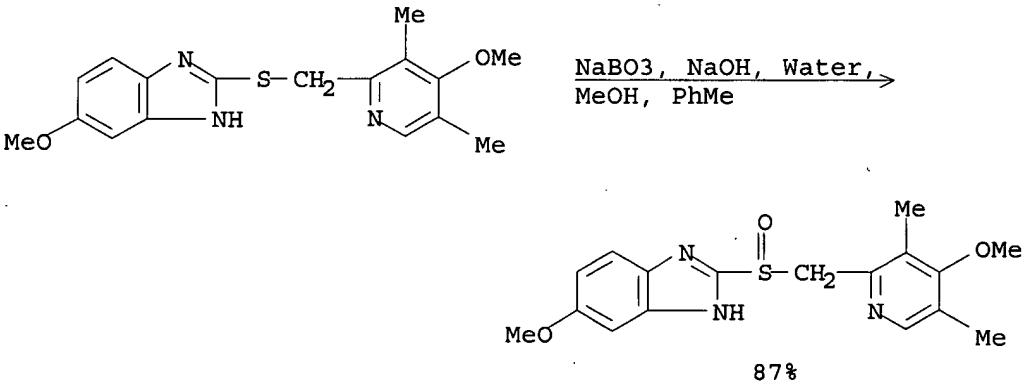
OTHER SOURCE(S): MARPAT 131:228722
GI



I

AB Title compds. [I; (a) R1, R3 = Me; R2, R4 = OMe; or (b) R1 = Me; R2 = OCH2CF3; R3, R4 = H; or (c) R1, R2 = OMe; R3 = H; R4 = OCHF2] were prepared by treatment of the corresponding methylthio compds. with a perborate salt in a liquid diluent at pH 7.5-14 at 0° to reflux. Thus, 5-methoxy-2-[[(4-methoxy-3,5-dimethylpyridin-2-yl)methyl]thio]-1H-benzimidazole in refluxing MeOH/PhMe was treated dropwise with a solution of NaOH and NaBO3 in H2O to give 86.5% 5-methoxy-2-[[(4-methoxy-3,5-dimethylpyridin-2-yl)methyl]sulfinyl]-1H-benzimidazole.

RX(1) OF 2



87%

NOTE: reflux

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 70 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 131:5258 CASREACT
TITLE: New process for the synthesis of omeprazole
INVENTOR(S): Cotton, Hanna; Larsson, Magnus; Mattson, Anders
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925711	A1	19990527	WO 1998-SE1984	19981103

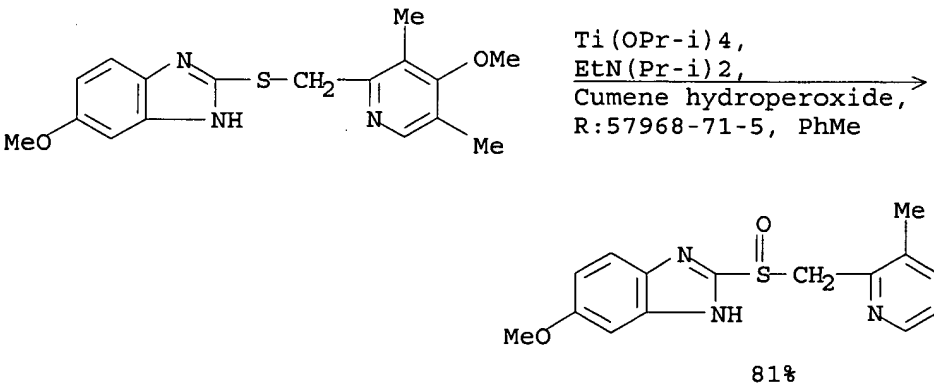
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,

TT, UA, UG, US, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

ZA 9809999	A	19990617	ZA 1998-9999	19981102
IN 190801	A1	20030823	IN 1998-DE3213	19981102
TW 588046	B	20040521	TW 1998-87118172	19981102
CA 2276753	A1	19990527	CA 1998-2276753	19981103
AU 9910582	A	19990607	AU 1999-10582	19981103
AU 750743	B2	20020725		
EP 964859	A1	19991222	EP 1998-953132	19981103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 9901643	T1	20000121	TR 1999-1643	19981103
EE 9900391	A	20000417	EE 1999-391	19981103
EE 4154	B1	20031015		
BR 9806871	A	20000418	BR 1998-6871	19981103
NZ 336447	A	20010223	NZ 1998-336447	19981103
JP 2001508466	T	20010626	JP 1999-528277	19981103
HU 200003737	A2	20011028	HU 2000-3737	19981103
RU 2211218	C2	20030827	RU 1999-117541	19981103
US 6303788	B1	20011016	US 1998-194647	19981201
NO 9903298	A	19990702	NO 1999-3298	19990702
NO 318197	B1	20050214		
MX 9906369	A	20000731	MX 1999-6369	19990707
HR 990218	A1	20000831	HR 1999-218	19990713
PRIORITY APPLN. INFO.:			SE 1997-4183	19971114
			WO 1998-SE1984	19981103

AB A novel process for the synthesis of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole, known under the generic name omeprazole, was given. Omeprazole was prepared by oxidizing 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]thio]-1H-benzimidazole in an organic solvent with an oxidizing agent in the presence of a titanium complex and optionally in the presence of a base.

RX(1) OF 1



81%

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 71 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 130:223273 CASREACT
TITLE: Preparation of pyridinylmethylsulfinylbenzimidazoles
INVENTOR(S): Arakawa, Nobuo; Kuroda, Hirofumi
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11071370	A	19990316	JP 1998-179461	19980626
PRIORITY APPLN. INFO.:			JP 1997-170058	19970626

OTHER SOURCE(S): MARPAT 130:223273
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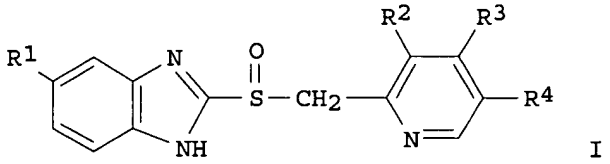

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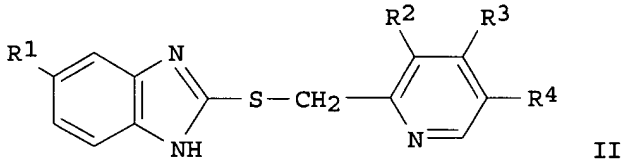
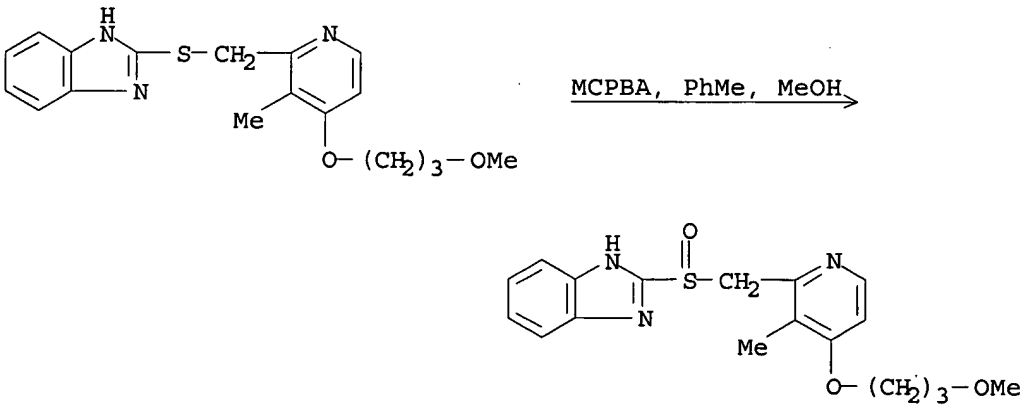


II

AB Title compds. I (R1 = H, OMe, OCHF2; R2 = Me, MeO; R3 = 3-methoxypropoxy, MeO, CF3CH2O; R4 = H, Me) were prepared by oxidation of thio ethers II (R1-R4 = same as above) with m-chloroperbenzoic acid in nonpolar solvents and lower alcs. Thus, oxidation of 2-{[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylthio}-1H-benzimidazole with m-chloroperbenzoic acid in toluene and methanol at -25° for 6.5 h gave 93.1% 2-{[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylsulfinyl}-1H-benzimidazole.

RX(1) OF 1



L2 ANSWER 72 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 130:196655 CASREACT
TITLE: Process for the preparation of omeprazole and intermediate compounds
INVENTOR(S): Baldwin, Jack Edward; Adlington, Robert Michael; Crouch, Nicholas Paul
PATENT ASSIGNEE(S): UK
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 899268	A2	19990303	EP 1998-306413	19980811
EP 899268	A3	19990707		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6043371	A	20000328	US 1998-131200	19980807
JP 11124376	A	19990511	JP 1998-227871	19980812
PRIORITY APPLN. INFO.:			GB 1997-17107	19970812

OTHER SOURCE(S): MARPAT 130:196655
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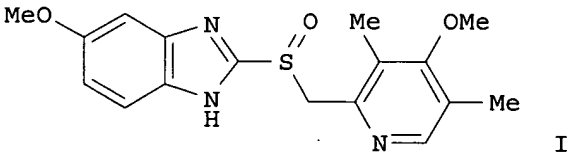

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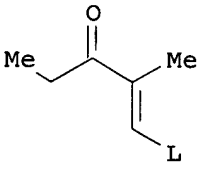
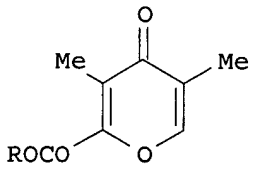


II

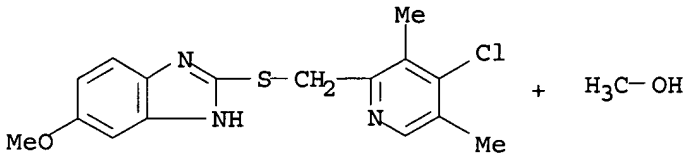


III

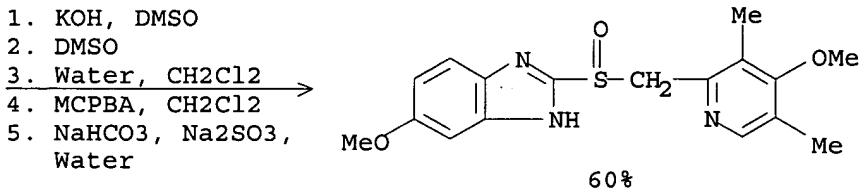
AB A strategy for synthesizing the gastric acid secretion inhibitor omeprazole (I), starting from 2-methyl-1-penten-3-on-1-ol (II; L = OH), is disclosed. The first 6 individual steps of the method, and most of the intermediate compds., are also claimed as new. Advantages include crystalline and low-toxicity intermediates, favorable reactions, and high yields. Thus, II (L = OH) was condensed with pyrrolidine in the presence of AcOH in benzene to give 75% II (L = pyrrolidino). This was condensed with oxalyl chloride and then MeOH or EtOH to give the pyrone esters III [R = Me (62%) or Et (39%)], which were then reduced by NaBH4 to the corresponding (hydroxymethyl)pyrone in 92% or 83% yield, resp. This pyrone alc. was treated with aqueous NH3 to give the corresponding pyridone alc. (96%), which was treated with POCl3 to give 4-chloro-2-(chloromethyl)-3,5-dimethylpyridine (IV) in 88% yield. Dichloride IV underwent a sequence of thioetherification with 5-methoxy-2-mercaptobenzimidazole at

the chloromethyl group (96%), methoxylation at the ring chloride, and finally S-oxidation using MCPBA (60% for 2 steps, with purification), to give I.

RX(8) OF 37



(step 2)



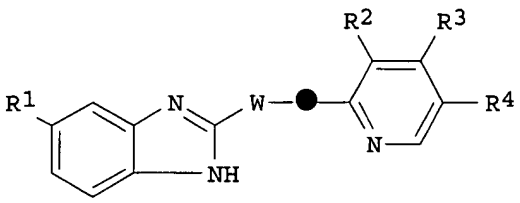
60%

L2 ANSWER 73 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 130:95552 CASREACT
TITLE: Processes for the preparation of pyridine derivatives
INVENTOR(S): Tagami, Katsuya; Niikawa, Nobuo; Kayano, Akio; Kuroda, Hirofumi
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902521	A1	19990121	WO 1998-JP3113	19980710
W: CA, CN, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 11071371	A	19990316	JP 1997-197119	19970723
CA 2295817	A1	19990121	CA 1998-2295817	19980710
JP 11171884	A	19990629	JP 1998-196379	19980710
EP 997461	A1	20000503	EP 1998-931055	19980710
EP 997461	B1	20030521		
R: DE, FR, GB, IT, SE				
EP 1300406	A1	20030409	EP 2003-566	19980710
EP 1300406	B1	20041006		
R: DE, FR, GB, IT, SE				
JP 2000016992	A	20000118	JP 1998-207399	19980723
US 6313303	B1	20011106	US 2000-462180	20000103

PRIORITY APPLN. INFO.:
JP 1997-186095 19970711
JP 1997-197119 19970723
JP 1998-117706 19980428
EP 1998-931055 19980710
WO 1998-JP3113 19980710

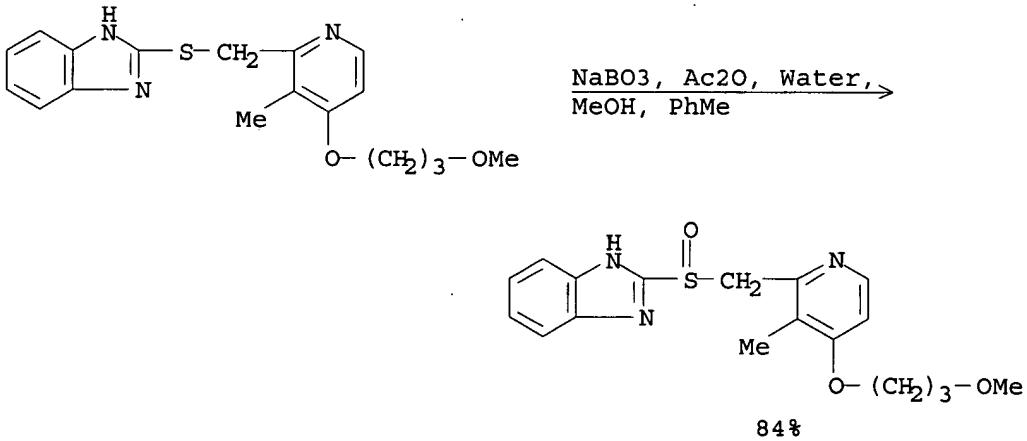
OTHER SOURCE(S): MARPAT 130:95552
GI



I

AB Characterized is a processes for preparing sulfoxides useful as drugs such as acid secretion inhibitors or antiulcer drugs or intermediates for the preparation of drugs in high yields at high purities. Specifically, the title compds. (I; W is SO; R1 is hydrogen, methoxy or difluoromethoxy; R2 is Me or methoxy; R3 is 3-methoxypropoxy, methoxy or 2,2,2-trifluoroethoxy; and R4 is hydrogen or Me) are prepared by oxidizing the thio ethers I (W is S, R1-R4 are as same as above) with a peroxoborate salt in the presence of an acid anhydride or a metal catalyst, or with an N-halosuccinimide, 1,3-dihalo-5,5-dimethyl-hydantoin or dichloroisocyanuric acid salt in the presence of a base. I [W = S, R1 = R4 = H, R2 = Me, R3 = O(CH2)3OMe] was oxidized by sodium peroxoborate in the presence of Ac2O to give 83.6% I [W = SO, R1 = R4 = H, R2 = Me, R3 = O(CH2)3OMe].

RX(1) OF 1



NOTE: -20.degree. for 2.5 h

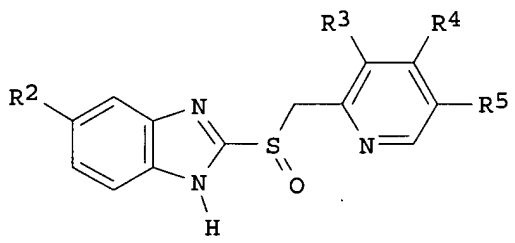
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 74 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 129:260458 CASREACT
TITLE: Process for the preparation of 2-[[(2-pyridinyl)methyl]sulfinyl]-1H-benzimidazoles
INVENTOR(S): Clausen, Finn Priess
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

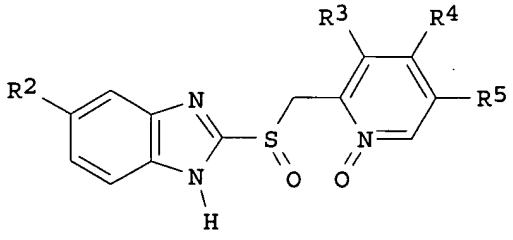
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840377	A1	19980917	WO 1998-DK58	19980216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9859821	A	19980929	AU 1998-59821	19980216
EP 968204	A1	20000105	EP 1998-902960	19980216
R: DE, DK, FI				
NO 9904209	A	19990831	NO 1999-4209	19990831
PRIORITY APPLN. INFO.:			DK 1997-251	19970307
			WO 1998-DK58	19980216

OTHER SOURCE(S): MARPAT 129:260458

GI



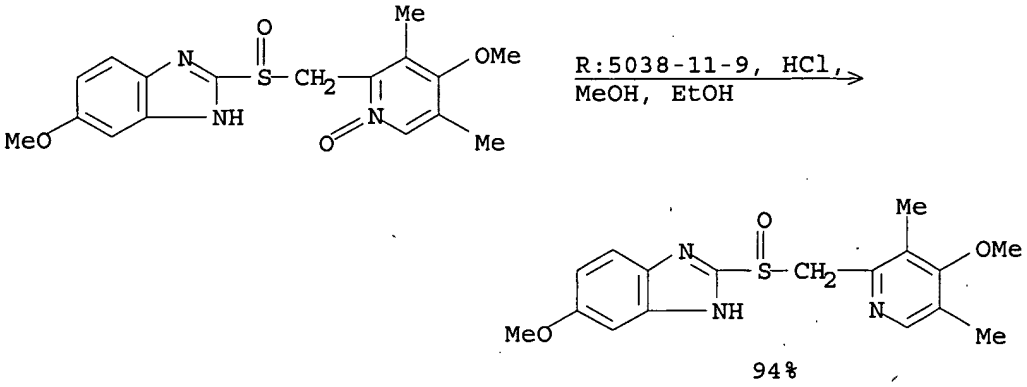
I



II

AB The title compds. [I; R2 = H, OMe, OCHF2, CF3; R3 = H, Me, OMe; R4 = H, OMe, OCH2CF3, halo; R5 = H, Me, OMe] such as Omeprazole, which are biol. active (no data) and/or may be used as intermediates in the synthesis of biol. active compds, were prepared by reducing a compound II with a thiobisamine such as thiobismorpholine or thiobispiperidine in the presence of a mineral acid.

RX(1) OF 2



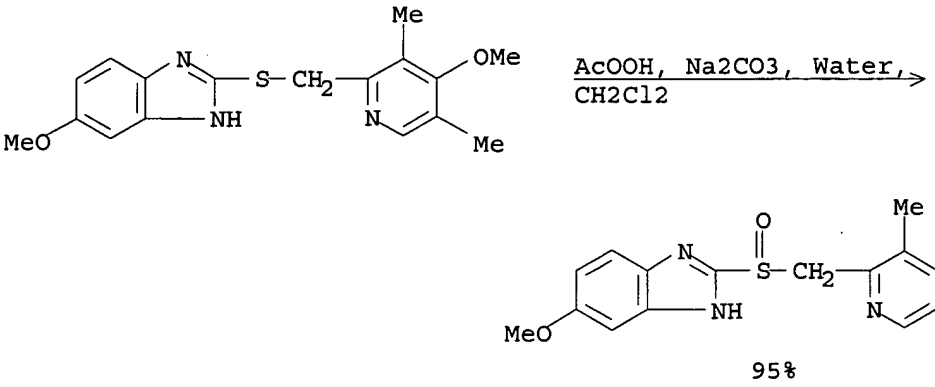
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 75 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 128:204887 CASREACT
TITLE: Method of omeprazole preparation
INVENTOR(S): Smahovsky, Vendel; Oremus, Vladimir; Heleyova, Katarina; Zlatoidsky, Pavol; Gattnar, Ondrej; Varga, Ivan; Stalmach, Valdemar; Jezek, Ladislav
PATENT ASSIGNEE(S): Slovakofarma, A.S., Slovakia
SOURCE: PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809962	A1	19980312	WO 1997-SK8	19970908
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
SK 283805	B6	20040203	SK 1996-1155	19960909
CA 2265538	A1	19980312	CA 1997-2265538	19970908
AU 9743253	A	19980326	AU 1997-43253	19970908
EP 931076	A1	19990728	EP 1997-941314	19970908
R: AT, CH, DE, ES, LI, SE, PT				
HU 9903744	A2	20000528	HU 1999-3744	19970908
CZ 293946	B6	20040818	CZ 1999-792	19970908
IN 186456	A1	20010901	IN 1997-DE3039	19971023
US 6229021	B1	20010508	US 1999-254414	19990305
PRIORITY APPLN. INFO.:			SK 1996-1155	19960909
			WO 1997-SK8	19970908

AB Omeprazole was prepared in 95% yield by a reaction of 5-methoxy-2-[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methylthio]-1H- benzimidazole with peroxyacetic acid in a two-phase H2O and chlorinated organic solvent medium (such as CH2Cl2) at alkaline pH.

RX(1) OF 1



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 76 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 128:22909 CASREACT
TITLE: Process for the preparation of a magnesium salt of a substituted sulfinyl heterocycle
INVENTOR(S): Hogberg, Jan-Ake; Ioannidis, Panagiotis; Mattson, Anders
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.; Hogberg, Jan-Ake; Ioannidis, Panagiotis; Mattson, Anders
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9741114	A1	19971106	WO 1997-SE674	19970422
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
SE 9601598	A	19971027	SE 1996-1598	19960426
SE 508669	C2	19981026		
ZA 9703153	A	19971027	ZA 1997-3153	19970414
TW 420676	B	20010201	TW 1997-86104766	19970414
HR 970210	B1	20020630	HR 1997-210	19970421
CA 2251636	A1	19971106	CA 1997-2251636	19970422
CA 2251636	C	20010410		
AU 9727193	A	19971119	AU 1997-27193	19970422
AU 711345	B2	19991014		
EP 897386	A1	19990224	EP 1997-921045	19970422
EP 897386	B1	20020828		
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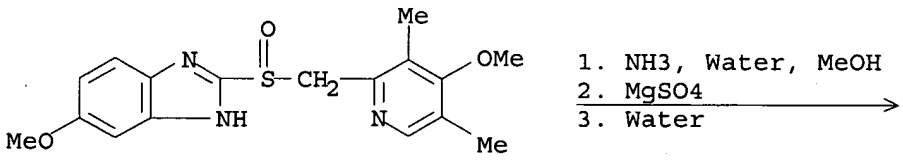
CN 1216989	A	19990519	CN 1997-194114	19970422
CN 1100776	B	20030205		
BR 9708829	A	19990803	BR 1997-8829	19970422

HU 9901798	A2	20000428	HU 1999-1798	19970422
JP 2000509067	T	20000718	JP 1997-538796	19970422
RU 2163238	C2	20010220	RU 1998-121016	19970422
EE 3485	B1	20010815	EE 1998-363	19970422
NZ 332154	A	20020301	NZ 1997-332154	19970422
AT 222904	T	20020915	AT 1997-921045	19970422
SK 282752	B6	20021203	SK 1998-1407	19970422
PT 897386	T	20021231	PT 1997-921045	19970422
ES 2180981	T3	20030216	ES 1997-921045	19970422
IL 126716	A	20031031	IL 1997-126716	19970422
PL 188824	B1	20050429	PL 1997-329683	19970422
CZ 295067	B6	20050518	CZ 1998-3398	19970422
US 6124464	A	20000926	US 1997-860825	19970710
NO 9804903	A	19981021	NO 1998-4903	19981021
NO 318850	B1	20050518		
HK 1016978	A1	20030221	HK 1999-102051	19990507
PRIORITY APPLN. INFO.:			SE 1996-1598	19960426
			WO 1997-SE674	19970422

OTHER SOURCE(S): MARPAT 128:22909

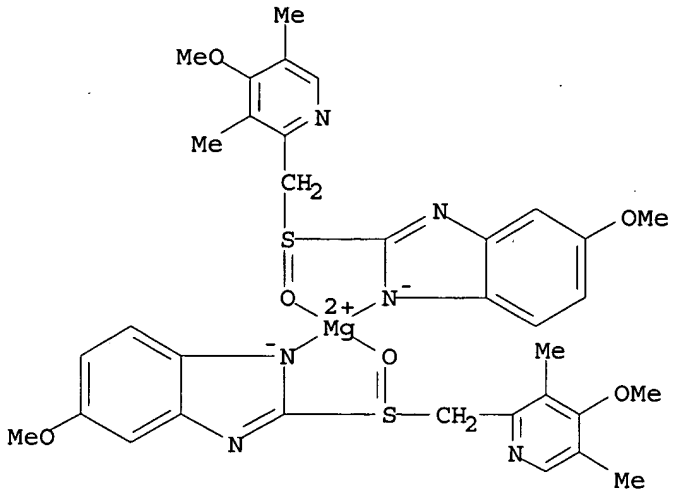
AB A novel process for the preparation of a magnesium salt of a substituted sulfinyl heterocyclic compound containing an imidazole moiety is described.. The process is carried out by mixing the substituted heterocycle with a weak base and a magnesium source. The base and the magnesium source are selected to result in residues which are easy to remove during the reaction. The invention also relates to the use of the compds. obtained in medicine. Thus, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium salt was obtained by the reaction of the corresponding free base with aqueous NH3 and MgSO4.7H2O in MeOH solution

RX(1) OF 1



(step 1)

RX(1) OF 1



71%

NOTE: the use of weak bases and other magnesium sources is also claimed

L2 ANSWER 77 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 126:46780 CASREACT

TITLE: Preparation and absolute configurations of optical isomers of sodium 2-[[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylsulfinyl]-1H-benzimidazole (E3810)

AUTHOR(S): Nochi, Shigeharu; Kawai, Takatoshi; Kawakami, Yoshiyuki; Asakawa, Naoki; Ueda, Norihiro; Hayashi, Kenji; Souda, Shigeru

CORPORATE SOURCE: Tsukuba Res. Labs., Eisai Co., Ltd., Ibaraki, 300-26, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (1996), 44(10), 1853-1857
CODEN: CPBTAL; ISSN: 0009-2363

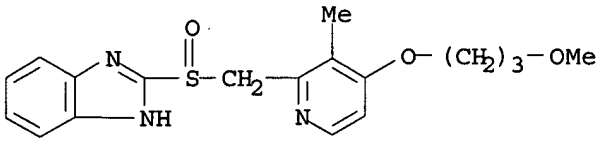
PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

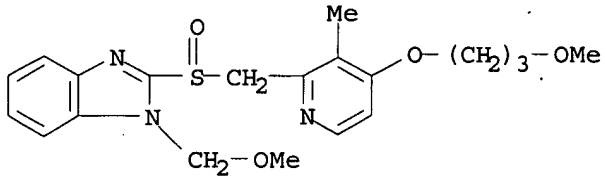
AB The optical isomers of sodium 2[[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylsulfinyl]-2H-benzimidazole (E3810), a proton pump inhibitor, were separated by HPLC and their absolute configurations were determined by x-ray crystallog. anal.

RX(1) OF 1



MeOCH2Cl, Et3N, DMF

Na



78%

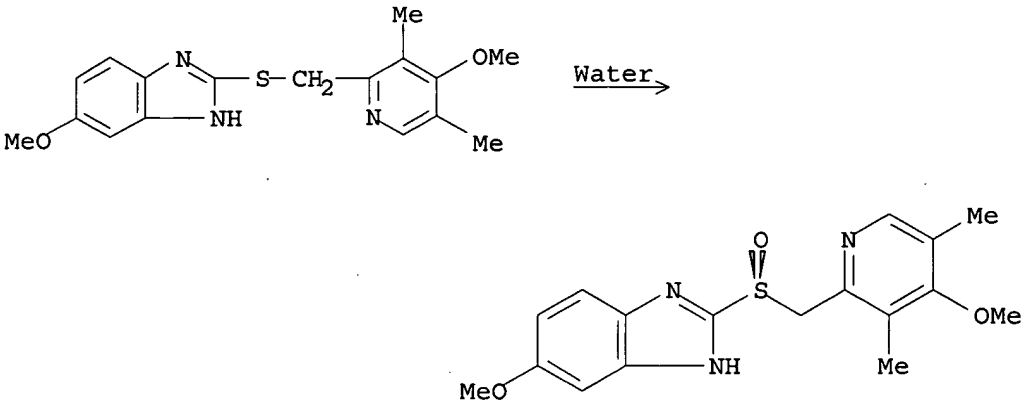
L2 ANSWER 78 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 125:112926 CASREACT
TITLE: Enantioselective preparation of pharmaceutically active sulfoxides by biooxidation
INVENTOR(S): Holt, Robert; Lindberg, Per; Reeve, Christopher; Taylor, Stephen
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9617076	A1	19960606	WO 1995-SE1415	19951127
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2203999	A1	19960606	CA 1995-2203999	19951127
AU 9641269	A	19960619	AU 1996-41269	19951127
AU 699577	B2	19981210		
EP 795024	A1	19970917	EP 1995-939460	19951127
EP 795024	B1	20030219		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10510705	T	19981020	JP 1996-518669	19951127
JP 3684576	B2	20050817		
AT 232907	T	20030315	AT 1995-939460	19951127
ES 2191066	T3	20030901	ES 1995-939460	19951127
US 5840552	A	19981124	US 1996-569114	19961121
PRIORITY APPLN. INFO.:			GB 1994-23970	19941128
			WO 1995-SE1415	19951127

OTHER SOURCE(S): MARPAT 125:112926
AB Pharmaceutically active sulfoxide stereoisomers are produced from the

corresponding sulfides by microbial oxidation Thus, (-)-omeprazole was produced in >99% enantiomeric excess by oxidation of the sulfide with Penicillium frequentans.

RX(1) OF 4



NOTE: BIOTRANSFORMATION, BIOOXIDATION, CELLS OF USTILAGO MAYDIS BPFC 6333, PHOSPHATE BUFFER, STEREOSELECTIVE

L2 ANSWER 79 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 125:58516 CASREACT
TITLE: Preparation of unsymmetrical heterocyclylsulfoxide enantiomers
INVENTOR(S): Larsson, Erik Magnus; Stenhede, Urban Jan; Soerensen, Henrik; Von Unge, Per Oskar Sverker; Cotton, Hanna Kristina
PATENT ASSIGNEE(S): Astra Aktiebolag, Swed.
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

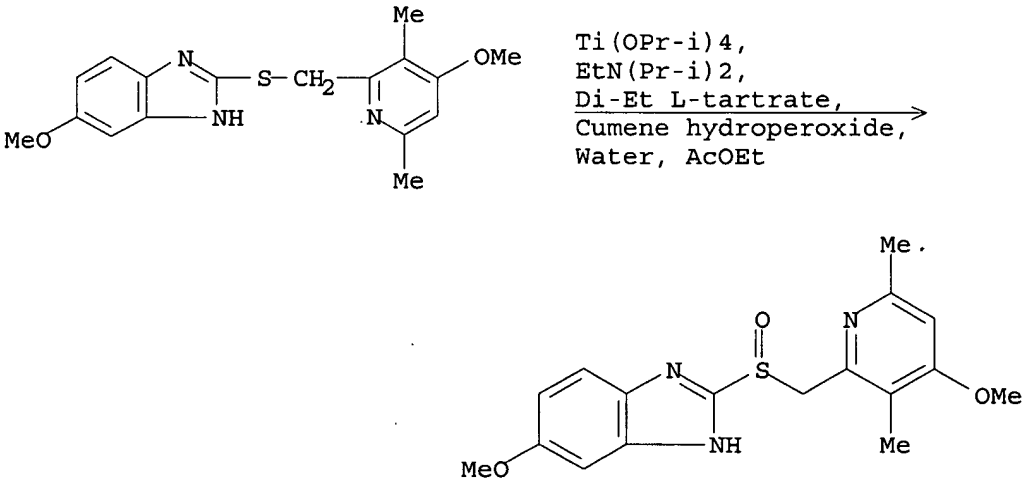
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9602535	A1	19960201	WO 1995-SE818	19950703
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
SE 9402510	A	19960116	SE 1994-2510	19940715
SE 504459	C2	19970217		
JP 10504290	T	19980428	JP 1996-504938	19950703
JP 3795917	B2	20060712		
RU 2157806	C2	20001020	RU 1997-102162	19950703
EE 3354	B1	20010215	EE 1997-6	19950703
AT 242233	T	20030615	AT 1995-926068	19950703
PT 773940	T	20031031	PT 1995-926068	19950703
ES 2199998	T3	20040301	ES 1995-926068	19950703
SK 284059	B6	20040908	SK 1997-48	19950703
CA 2193994	A1	19960201	CA 1995-2193994	19950705
CA 2193994	C	20050503		

AU 9529948	A	19960216	AU 1995-29948	19950705
AU 688074	B2	19980305		
EP 773940	A1	19970521	EP 1995-926068	19950705
EP 773940	B1	20030604		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1157614	A	19970820	CN 1995-194956	19950705
CN 1070489	B	20010905		
HU 76642	A2	19971028	HU 1997-108	19950705
BR 9508292	A	19971223	BR 1995-8292	19950705
PL 186342	B1	20031231	PL 1995-318165	19950705
IN 1995DE01255	A	20050701	IN 1995-DE1255	19950705
IL 114477	A	20010724	IL 1995-114477	19950706
ZA 9505724	A	19960115	ZA 1995-5724	19950710
HR 950401	B1	20040430	HR 1995-401	19950712
US 5948789	A	19990907	US 1995-492087	19950714
FI 9700102	A	19970110	FI 1997-102	19970110
NO 9700153	A	19970114	NO 1997-153	19970114
NO 312101	B1	20020318		
HK 1008331	A1	20031121	HK 1998-109230	19980717
PRIORITY APPLN. INFO.:			SE 1994-2510	19940715
			WO 1995-SE818	19950703

OTHER SOURCE(S): MARPAT 125:58516

AB Enantiomeric R1ZSOR2 [R1 = (un)substituted 2-pyridyl, (un)substituted 2-(R4R5N)C6H4; R2 = (un)substituted 2-benzimidazolyl, thieno[3,4-d]imidazol-2-yl, etc.; R4,R5 = H, (ar)alkyl; Z = CH2, (un)substituted 1,2-phenylene, etc.] were prepared by oxidation of prochiral R1ZSR2 in the presence of a chiral Ti complex and a base.

RX(1) OF 1



Na

47%

NOTE: 99.8% e.e.

L2 ANSWER 80 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 123:228183 CASREACT

TITLE: New process for the synthesis of a 2-(2-pyridylmethylsulfinyl)benzimidazole derivative

[lansoprazole], and new intermediates prepared in the process.

INVENTOR(S): Buxade Vinas, antonio
PATENT ASSIGNEE(S): Laboratorios Vinas, S.A., Spain

SOURCE: Span., 15 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2060541	A1	19941116	ES 1993-384	19930226
ES 2060541	B1	19951116		

PRIORITY APPLN. INFO.: ES 1993-384 19930226

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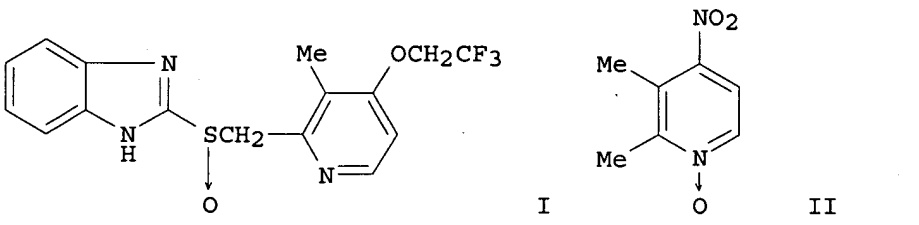
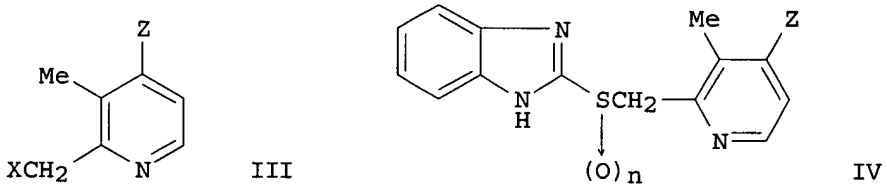


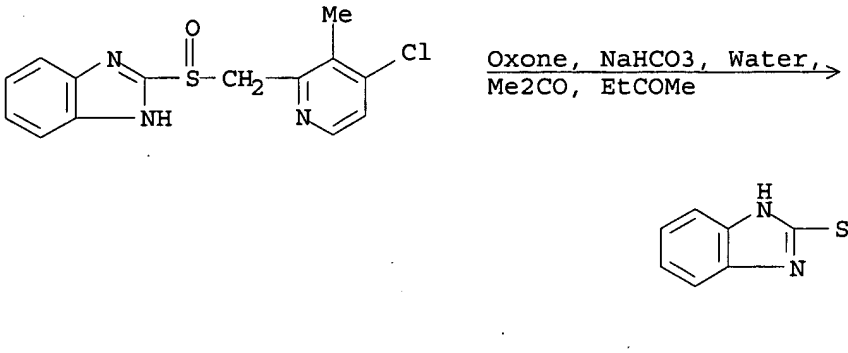
I II



III IV

AB The antisecretory agent lansoprazole (I) is prepared by a new, more economical, and less toxic process, in 3-4 steps starting from 2,3-dimethyl-4-nitropyridine N-oxide (II). For example, reaction of II with CCl3COCl in refluxing CHCl3, followed by NaOH in MeOH, and then workup and treatment with excess refluxing SOCl2, gave 55% 4-chloro-2-chloromethyl-3-methylpyridine [III; X = Z = Cl]. Reaction of III [X = Cl, Br; Z = halo, NO2] with 2-mercaptobenzimidazole and NaOH in aqueous MeOH gave >85% sulfides IV [Z = Cl, Br, NO2; n = 0]. Oxidation of the latter with potassium peroxymonosulfate (62-76%) or with H2O2 and Mo or V acetylacetonate catalysts (71-82%) gave IV [Z = Cl, Br, NO2; n = 1]. These reacted with CF3CH2OH and NaH in DMSO to give I in 72% (Z = Cl), 80% (Z = Br), or 48% (Z = NO2) yield.

RX(1) OF 9

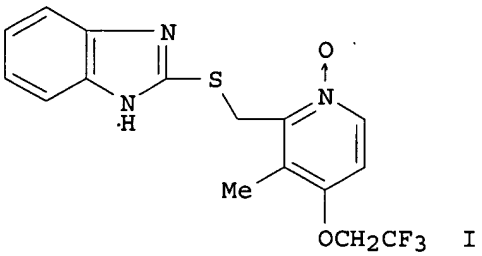


76%

L2 ANSWER 81 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 122:290859 CASREACT
TITLE: Process and catalysts for the preparation of 2-[[(1H-benzimidazol-2-yl)thio]methyl]-3-methyl-4-(2,2,2-trifluoroethoxy)pyridinium N-oxide as an intermediate for lansoprazole bulk manufacture
INVENTOR(S): Monserrat Vidal, Carlos; Serra, Marcia, Xavier
PATENT ASSIGNEE(S): Laboratorios S.A.L.V.A.T., S.A., Spain
SOURCE: Span., 13 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2063705	A1	19950101	ES 1993-1312	19930614
ES 2063705	B1	19950716		

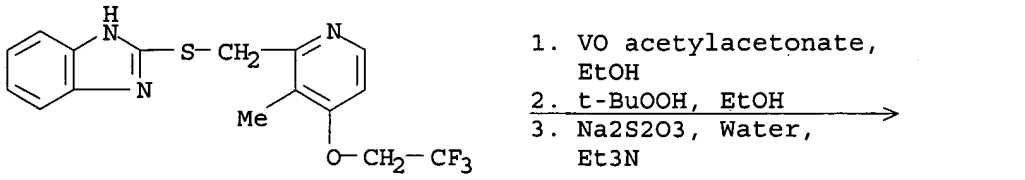
PRIORITY APPLN. INFO.: ES 1993-1312 19930614
GI



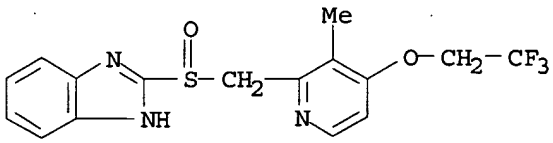
I

AB The title compound, I, is prepared from 2,3-dimethyl-4-nitropyridinium N-oxide in 3 steps and is used as an intermediate for the industrial-scale preparation of lansoprazole.

RX(6) OF 13



(step 1)

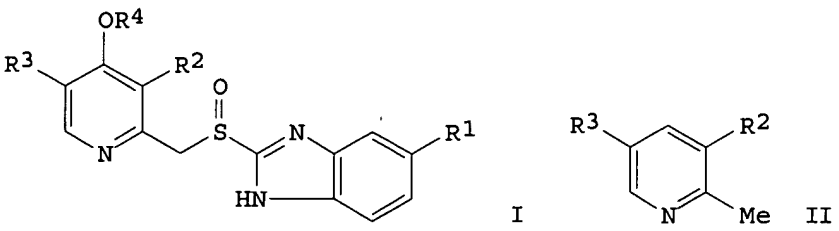


95%

L2 ANSWER 82 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 120:107017 CASREACT
TITLE: Process for preparation of benzimidazole-containing derivatives of pyridine [e.g., lansoprazole]
INVENTOR(S): Palomo Coll, Alberto
PATENT ASSIGNEE(S): Centro Genesis para la Investigacion S.L., Spain
SOURCE: Span., 34 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2036948	A1	19930601	ES 1991-2594	19911121
ES 2036948	B1	19940901		
ES 2066701	A1	19950301	ES 1993-64	19930115
ES 2066701	B1	19951201		
ES 2067407	A1	19950316	ES 1993-935	19930504
ES 2067407	B1	19960416		
ES 2105953	A1	19971016	ES 1994-2419	19941124
ES 2105953	B1	19980701		

PRIORITY APPLN. INFO.: ES 1991-2594 19911121
OTHER SOURCE(S): MARPAT 120:107017
GI



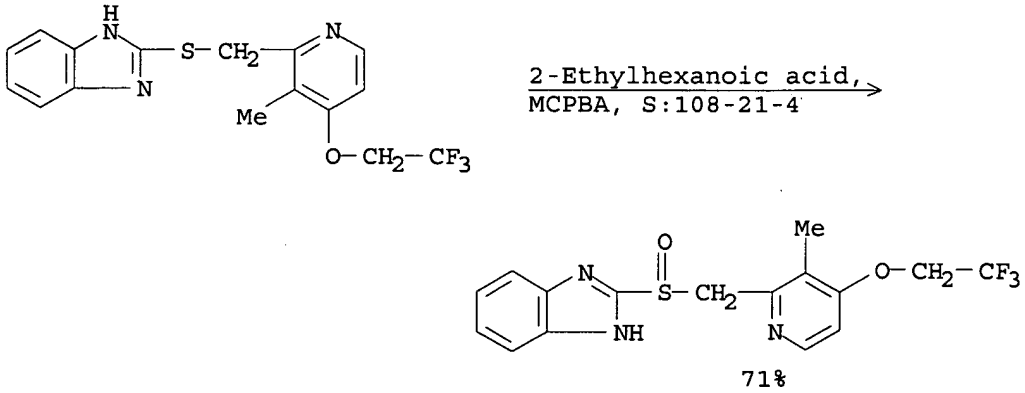
I

II

AB Pyridine derivs. I [X = CH, N; R1 = H, OMe, OCHF2, OCH2CF3, OCHMe2, OCH2CHMe2, cyclopropylmethoxy; R2, R3 = H, Me, OMe; R4 = CH2CF3, Et, CHMe2, Me, (CH2)3OMe; except case of X = CH, R1 = OMe, R2-R4 = Me], used

as antiulcer agents (no data), are prepared in a min. of 7 steps from simple pyridines II by several synthetic variations. For example, 2,3-dimethylpyridine underwent N-oxidation and 4-nitration (95%), monochlorination of the 2-Me group (95%), N-reduction and conversion to the HCl salt (87%), thioetherification of the CH2Cl group with 2-mercaptobenzimidazole (87%), Pd(PPh3)4-catalyzed displacement of nitro by CF3CH2OH (90%), and S-oxidation (75%) to give I [X = CH, R1 = R3 = H, R2 = Me, R4 = CH2CF3], i.e. lansoprazole.

RX(16) OF 60



NOTE: 0-5.degree.

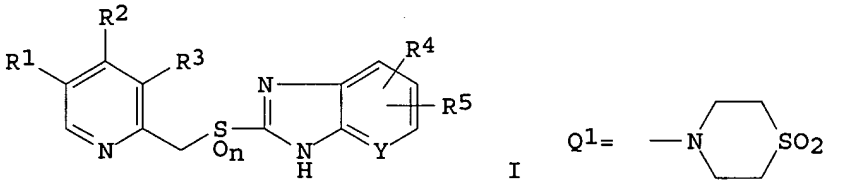
L2 ANSWER 83 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 119:8812 CASREACT
TITLE: Oxidation of benzimidazolylthiomethylpyridines and related compounds to benzimidazolyl sulfinylmethylpyridines using magnesium monoperoxyphthalate
INVENTOR(S): Hoerrner, Robert Scott; Friedman, Joel J.; Amato, Joseph Sebastian; Liu, Thomas Meng Han; Shinkai, Ichiro; Weinstock, Leonard M.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 533264	A1	19930324	EP 1992-202792	19920912
EP 533264	B1	19991110		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
WO 9306097	A1	19930401	WO 1992-US7712	19920911
W: BG, CS, FI, HU, NO, PL, RO, RU				
AT 186535	T	19991115	AT 1992-202792	19920912
ES 2143468	T3	20000516	ES 1992-202792	19920912
PT 533264	T	20000531	PT 1992-202792	19920912
JP 05213936	A	19930824	JP 1992-244822	19920914
JP 07020956	B	19950308		
IL 103156	A	19970218	IL 1992-103156	19920914
ZA 9207034	A	19930329	ZA 1992-7034	19920915
CA 2078517	A1	19930321	CA 1992-2078517	19920917
CA 2078517	C	20031104		

AU 9225207	A	19930325	AU 1992-25207	19920918
AU 649355	B2	19940519		
CN 1071169	A	19930421	CN 1992-110899	19920919
CN 1048729	B	20000126		
US 5391752	A	19950221	US 1993-22804	19930222
GR 3032619	T3	20000531	GR 2000-400318	20000209
PRIORITY APPLN. INFO.:			US 1991-764564	19910920
			US 1991-777873	19911015

OTHER SOURCE(S): MARPAT 119:8812

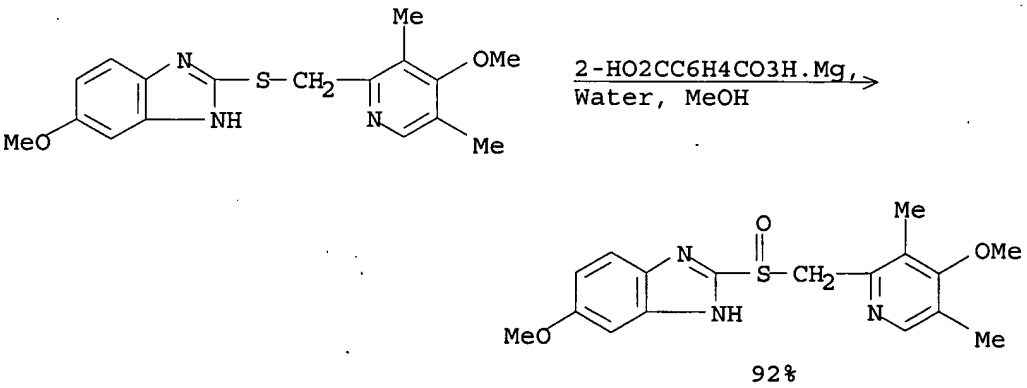
GI



I

AB Title compds. [I; R1, R3 = H, (cyclo)alkyl, fluoroalkyl, alkoxy; R2 = R1, O(CH2)m R6; R4, R5 = R1, CF3, alkoxycarbonyl; R6 = O(CH2)pR7, pyrrolidonyl, succinimidyl, 3,4-methylenedioxy, Q1, (substituted) Ph, etc.; R7 = H, alkoxy, (hetero)aryl, aryloxy, aralkoxy, halo, CO2H, alkoxycarbonyl, etc.; Y = CH, N; m, p = 1-5; n = 1], were prepared by treatment of the corresponding I (n = 0) with 0.5-0.7 molar equivalents of Mg monoperoxyphthalate. Thus, pyrmetazole in MeOH/H2O at -10° was treated dropwise with Mg monoperoxyphthalate in MeOH/H2O and the mixture was stirred at -10° for 35 min to give 92% omeprazole of 99.5% purity.

RX(1) OF 1



92%

NOTE: -10.degree., 35 min

L2 ANSWER 84 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

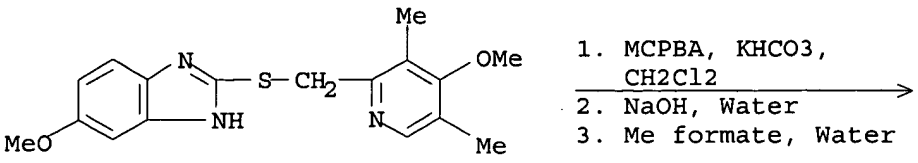
ACCESSION NUMBER:	116:128926 CASREACT
TITLE:	Method for synthesis of omeprazole
INVENTOR(S):	Braendstroem, Arne Elof
PATENT ASSIGNEE(S):	Astra AB, Swed.
SOURCE:	PCT Int. Appl., 11 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

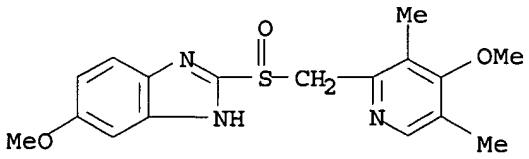
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9118895	A1	19911212	WO 1991-SE402	19910605
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
ZA 9103779	A	19920226	ZA 1991-3779	19910517
IL 98274	A	19950330	IL 1991-98274	19910527
CA 2083605	A1	19911208	CA 1991-2083605	19910605
CA 2083605	C	19981208		
AU 9180807	A	19911231	AU 1991-80807	19910605
AU 640246	B2	19930819		
EP 533752	A1	19930331	EP 1991-910929	19910605
EP 533752	B1	19980128		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 63408	A2	19930830	HU 1992-3855	19910605
HU 214323	B	19980302		
JP 05507699	T	19931104	JP 1991-510790	19910605
JP 2993122	B2	19991220		
PL 165433	B1	19941230	PL 1991-297169	19910605
RU 2061693	C1	19960610	RU 1992-16535	19910605
RO 111366	B1	19960930	RO 1992-1512	19910605
AT 162790	T	19980215	AT 1991-910929	19910605
ES 2113378	T3	19980501	ES 1991-910929	19910605
CZ 279928	B6	19950816	CZ 1991-1726	19910606
SK 278505	B6	19970806	SK 1991-1726	19910606
CN 1058211	A	19920129	CN 1991-103923	19910607
CN 1040536	B	19981104		
IN 178921	A1	19970719	IN 1991-DE412	19910613
HR 920770	B1	20000630	HR 1992-770	19921001
NO 9204682	A	19921204	NO 1992-4682	19921204
NO 300541	B1	19970616		
FI 102967	B	19990331	FI 1992-5529	19921204
FI 102967	B1	19990331		
US 5386032	A	19950131	US 1993-67406	19930525
LV 10271	B	19950420	LV 1993-1020	19930810
LT 3584	B	19951227	LT 1993-1711	19931230
PRIORITY APPLN. INFO.:			SE 1990-2043	19900607
			US 1991-708345	19910531
			WO 1991-SE402	19910605
			YU 1991-992	19910605

AB Omeprazole (I) was prepared in an improved process by treating 5-methoxy-2-[(4-methoxy-3,5,-dimethyl-2-pyridinyl)methylthio]-1H-benzimidazole (II) with m-ClC6H4C(O)OOH in CH2Cl2 at pH 8.0-8.6, extracting with aqueous NaOH, followed by addition of an alkyl formate to the aqueous phase resulting in crystallization of I. Thus, II was treated with m-ClC6H4C(O)OOH in CH2Cl2 at pH 8.6, which was maintained by KHCO3, at 0°, dilute NaOH was then added to a pH above 12 and its CH2Cl2 phase separated Me formate was added to the water phase and the pH kept above 9 and the omeprazole crystallized in 92% yield.

RX(1) OF 1



(step 1)



92%

L2 ANSWER 85 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 114:164100 CASREACT

TITLE: Studies on (H+-K+)-ATPase inhibitors of gastric acid secretion. Prodrugs of 2-[(2-pyridinylmethyl)sulfinyl]benzimidazole proton-pump inhibitors

AUTHOR(S): Sih, John C.; Wha bin Im; Robert, Andre; Graber, David R.; Blakeman, David P.

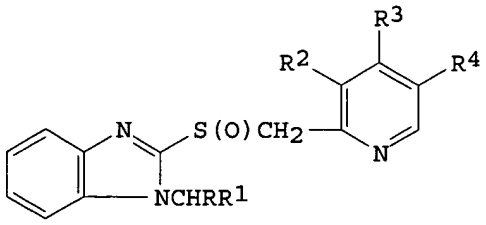
CORPORATE SOURCE: Res. Lab., Upjohn Co., Kalamazoo, MI, 49001, USA

SOURCE: Journal of Medicinal Chemistry (1991), 34(3), 1049-62
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

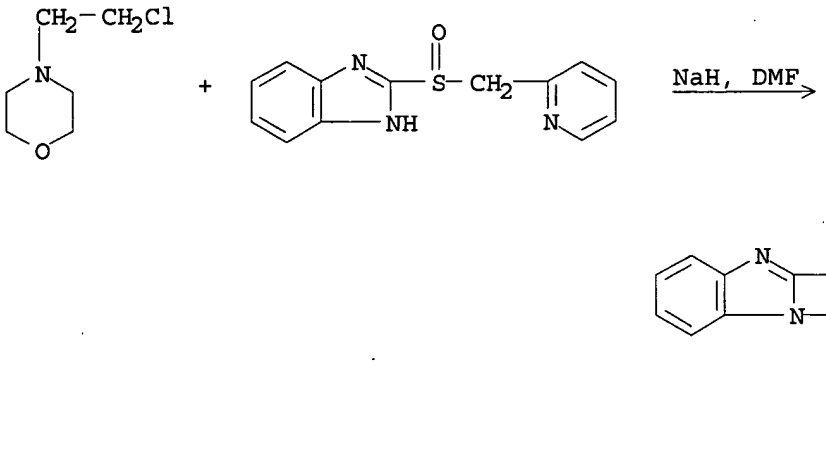


I

AB The synthesis of N-substituted benzimidazole (H+ -K+)-ATPase or proton-pump inhibitors is described. These compds. were prepared to function as prodrugs of the parent N-H compound and evaluated for their ability to inhibit gastric (H+-K+)-ATPase and gastric acid secretion. The products reported rely on either in vivo esterase hydrolysis for liberation of the parent compound or require an acid environment for release of the active drug. The N-(acyloxy)alkyl-substituted benzimidazoles I [R = H, R1 = AcO; R2 = R3 = R4 = H; R2 = Me, R3 = SEt, R4 = H; R2 = R4 = Me, R3 = OMe (II)] showed improved chemical stability in the solid state and in aqueous solns. when compared to their parent N-H compds. When given orally, II was found to be twice as potent as omeprazole in both the Shay rat and inactivation of gastric (H+-K+)-ATPase in the rat. The N-ethoxy-1-ethyl-substituted benzimidazoles I [R = Me, R1 = OEt; R2 = R3 = R4 = H (III); R2 = R4 = Me, R3 = OMe; R2 = Me, R3 = SEt, R4 = H] were found equally as effective as the N-H compound for inhibition of rat

(H+-K+)-ATPase activity. In the Shay rat III at 10 mg/kg was approx. twice as active as parent timoprazole.

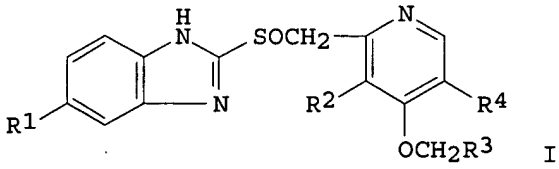
RX(2) OF 54



L2 ANSWER 86 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	114:94942 CASREACT
TITLE:	Synthesis of 2-[[(4-fluoroalkoxy-2-pyridyl)methyl]sulfinyl]-1H-benzimidazoles as antiulcer agents
AUTHOR(S):	Kubo, Keiji; Oda, Katsuaki; Kaneko, Tatsuhiko; Satoh, Hiroshi; Nohara, Akira
CORPORATE SOURCE:	Res. Dev. Div., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SOURCE:	Chemical & Pharmaceutical Bulletin (1990), 38(10), 2853-8 CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE:	Journal
LANGUAGE:	English

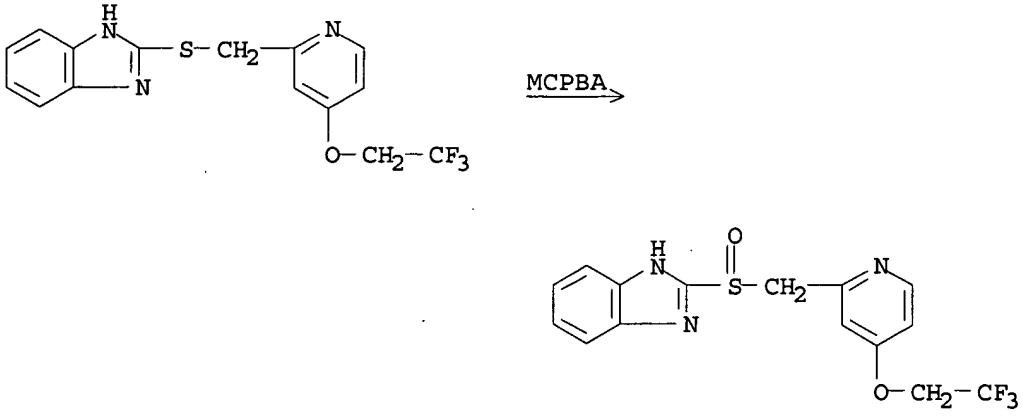
GI



I

AB Many title compds. (I, R1 = H, F, alkoxy, CF3 or MeSO2, R2 and R4 = H or Me, R3 = CF3, C2F5, HCF2CF2 or CCl3) were synthesized and tested for antisecretory, antiulcer, and cytoprotective activities. Most of these compds. were superior to omeprazole in antisecretory and antiulcer potencies, and especially in protecting the gastric mucosa from ethanol-induced damage. AG-1749 (Iansoprazole) (I, R1 = R4 = H, R2 = Me, R3 = CF3), was selected for further development and clin. evaluation.

RX(2) OF 40



L2 ANSWER 87 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 111:115102 CASREACT

TITLE: 2-[[(4-Amino-2-pyridyl)methyl]sulfinyl]benzimidazole H+/K+-ATPase inhibitors. The relationship between pyridine basicity, stability, and activity

AUTHOR(S): Ife, Robert J.; Dyke, Catherine A.; Keeling, David J.; Meenan, Eugene; Meeson, Malcolm L.; Parsons, Michael E.; Price, Carolyn A.; Theobald, Colin J.; Underwood, Anthony H.

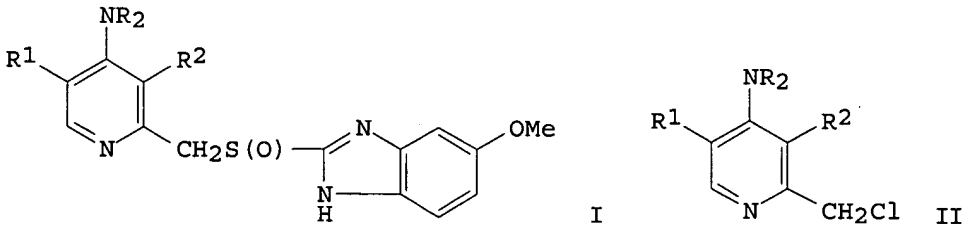
CORPORATE SOURCE: Smith Kline and French Res. Ltd., Welwyn/Hertfordshire, AL6 9AR, UK

SOURCE: Journal of Medicinal Chemistry (1989), 32(8), 1970-7
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



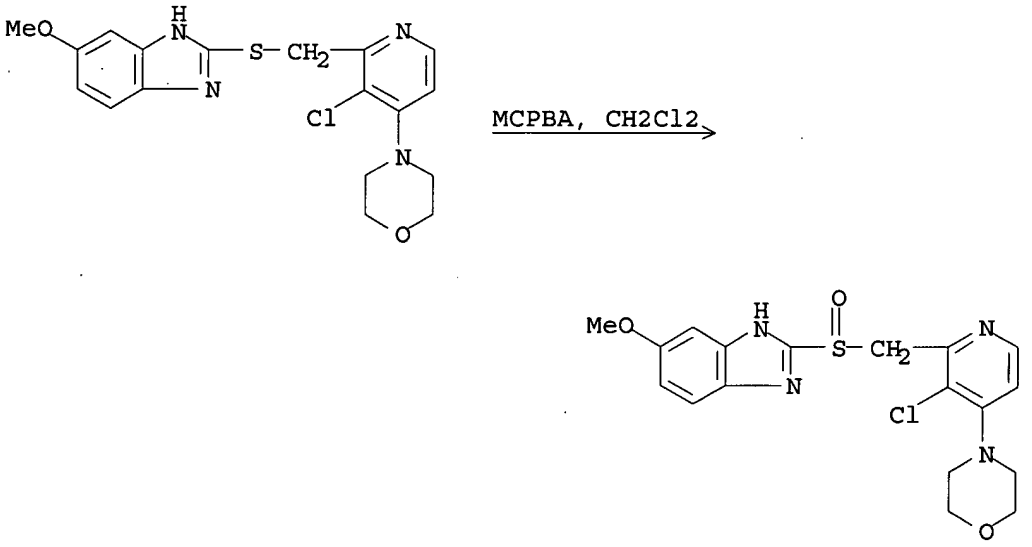
I

II

AB The benzimidazole sulfoxide class of antisecretory H+/K+-ATPase inhibitors need to possess high stability under neutral physiol. conditions yet rearrange rapidly at low pH to the active sulfenamide. Since the initial reaction involves internal nucleophilic attack by the pyridine nitrogen, control of the pyridine pKa is critical By utilizing the powerful electron-donating effect of a 4-amino substituent on the pyridine, moderated by the electron-withdrawing effect of a 3- or 5-halogen substituent, a combination of high potency (as inhibitors of histamine-stimulated gastric acid secretion) and good stability under physiol. conditions can be obtained in the title compds. I (NR2 = morpholino, NMe2, etc.; R1 = H, halo, Me; R2 = H, halo). Furthermore, the role of the steric interaction between the 3/5-substituents and the 4-substituent in modifying the electron-donating ability of the 4-amino

group is exemplified, and addnl. factors affecting stability are identified. One compound, in particular, 2-[[(3-chloro-4-morpholino-2-pyridyl)methyl]sulfinyl]-5-methoxy-(1H)-benzimidazole was chosen for further development and evaluation in man. I were prepared by reaction of aminopyridines II with 5-methoxy-2-mercaptobenzimidazole, followed by oxidation

RX(35) OF 86



68%

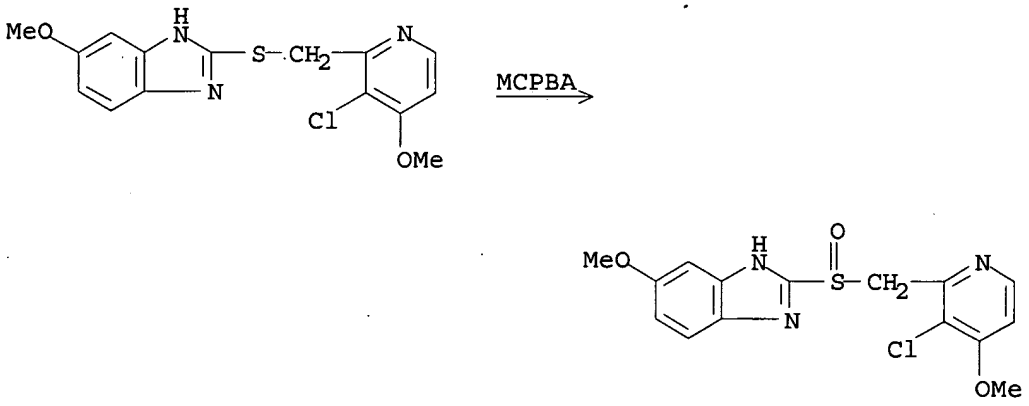
L2 ANSWER 88 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 111:7405 CASREACT
TITLE: Preparation of 2-(pyridylmethylthio)benzimidazoles and analogs as ulcer inhibitors and for treating diarrhea
INVENTOR(S): Lang, Hans Jochen; Weidmann, Klaus; Herling, Andreas W.
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 298440	A1	19890111	EP 1988-110774	19880706
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 3722810	A1	19890119	DE 1987-3722810	19870710
FI 8803251	A	19890111	FI 1988-3251	19880707
NO 8803047	A	19890111	NO 1988-3047	19880707
ZA 8804878	A	19890329	ZA 1988-4878	19880707
DK 8803840	A	19890111	DK 1988-3840	19880708
AU 8818884	A	19890112	AU 1988-18884	19880708
JP 01029374	A	19890131	JP 1988-169163	19880708
HU 48620	A2	19890628	HU 1988-3607	19880708
HU 200335	B	19900528		

PRIORITY APPLN. INFO.: DE 1987-3722810 19870710
OTHER SOURCE(S): MARPAT 111:7405
GI For diagram(s), see printed CA Issue.

AB The title compds. [I; R1 - R4 = H, halo, CN, NO2, (substituted) alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylcarbonyl, alkoxycarbonyl, carbamoyl, cycloalkyl, Ph, PhCH2, PhO, PhCH2O, PhNH, etc.; neighboring pairs of R1R4 = CH:CHCH:CH, (halo)alkylene; R5 = H, alkanoyl, alkylcarbonoyl, N-protecting group; R6, R7 = H, alkyl; R8, R10 = H, halo, alkyl, CF3, cycloalkyl, alkoxy, aralkoxy, amino, alkylmercapto, alkylsulfinyl, alkylsulfonyl; R9 = alkoxy, cycloalkyloxy, aralkoxy, alkylmercapto, alkylsulfinyl, alkylsulfonyl; T = S, SO, SO2], useful as ulcer inhibitors (no data), were prepared 3-Chloro-2-chloromethyl-4-methoxypyridine.HCl (preparation gives) was added to 5-methoxy-2-mercaptobenzimidazole in EtOH/aq NaOH at -10°. The mixture was stirred 1 h at room temperature to give 2-(3-chloro-4-methoxy-2-picolylmercapto)-5-methoxy-1H-benzimidazole.

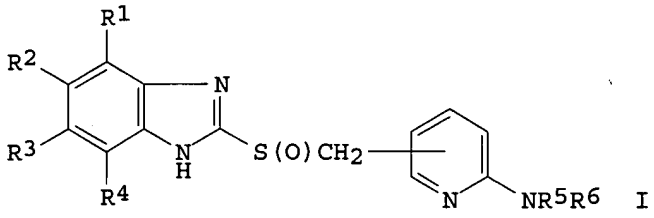
RX(3) OF 4



L2 ANSWER 89 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 110:135240 CASREACT
TITLE: Preparation of [(1H-benzimidazol-2-ylsulfinyl)methyl]-2-pyridinamines as antiulcer agents
INVENTOR(S): Adelstein, Gilbert W.; Moormann, Alan E.; Yu, Stella S. T.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: U.S., 14 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

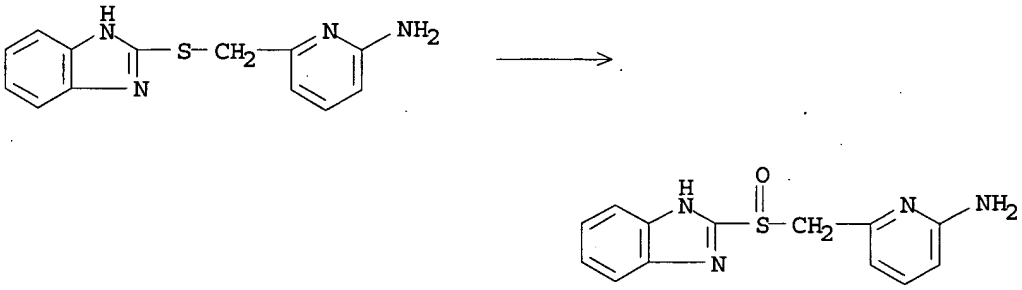
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4772619	A	19880920	US 1986-887780	19860717

PRIORITY APPLN. INFO.: US 1986-887780 19860717
OTHER SOURCE(S): MARPAT 110:135240
GI

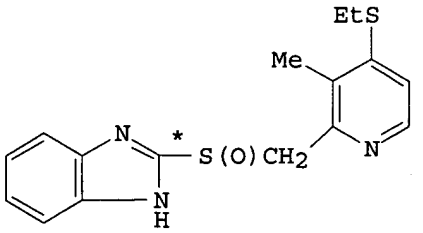


AB The title compds. [I; R1-R4 = H, C1-6 (hydroxy)alkyl, C1-4 fluoroalkyl, C1-6 alkoxy, halo; R5, R6 = H, C1-6 alkyl] and their pharmaceutically acceptable salts were prepared as inhibitors of gastric acid secretion, useful in treatment and prevention of ulcers. 6-Methyl-2-pyridinamine was N-acylated with Me3CCOCl and the product was brominated with N-bromosuccinimide in the presence of NCCMe2N:NCMe2CN to give N-[6-(bromomethyl)-2-pyridinyl]-2,2-dimethylpropanamide mixed with the dibromomethyl derivative The mixture was refluxed with 2-mercaptobenzimidazole in Me2CHOH and the product was deacylated by refluxing in 10% HCl to give 6-[(1H-benzimidazol-2--ylthio)methyl]-2-pyridinamine. The latter was oxidized with 3-ClC6H4C(O)OOH in CHCl3 at 0° to give I (R1-R6 = H) (II). II inhibited (H+ + K+)-ATPase with an IC50 of 2.5 mcM and in dogs 3 mg II/kg intraduodenally reduced gastric acid secretion 59%.

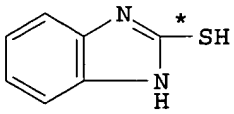
RX(5) OF 12



L2 ANSWER 90 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 110:95094 CASREACT
TITLE: Synthesis of carbon-14 labeled disuprazole
AUTHOR(S): Stolle, W. T.; Sih, J. C.; Hsi, R. S. P.
CORPORATE SOURCE: Res. Lab., Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(8), 891-900
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



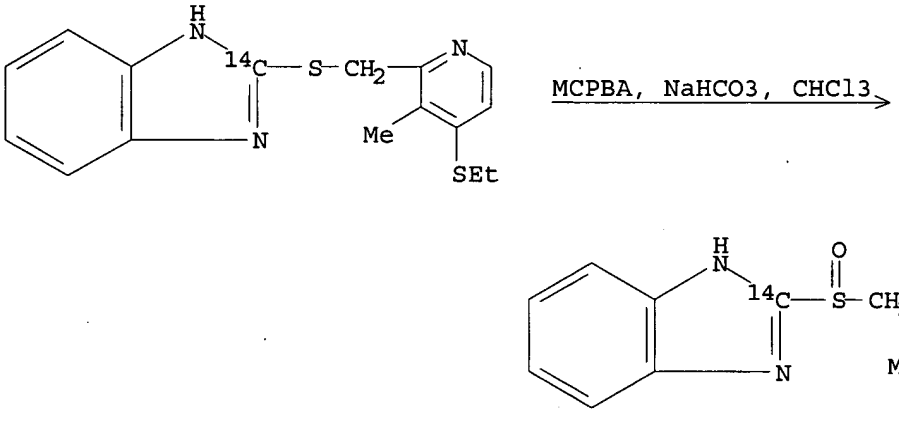
I



II

AB The title compound (I) was prepared from o-phenylenediamine. The diamine underwent a cyclocondensation with 14CS2 to give labeled benzimidazole II, II was etherified by a 2-pyridylmethyl mesylate derivative, and the sulfide obtained was oxidized by 3-ClC6H4C(O)OOH to give I.

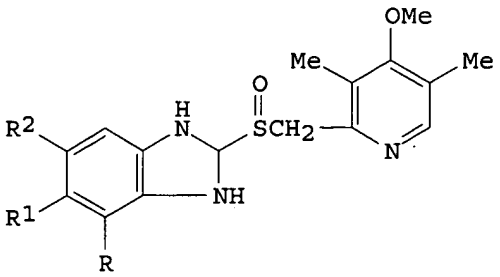
RX(10) OF 62



NOTE: 67% radiochem.

L2 ANSWER 91 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

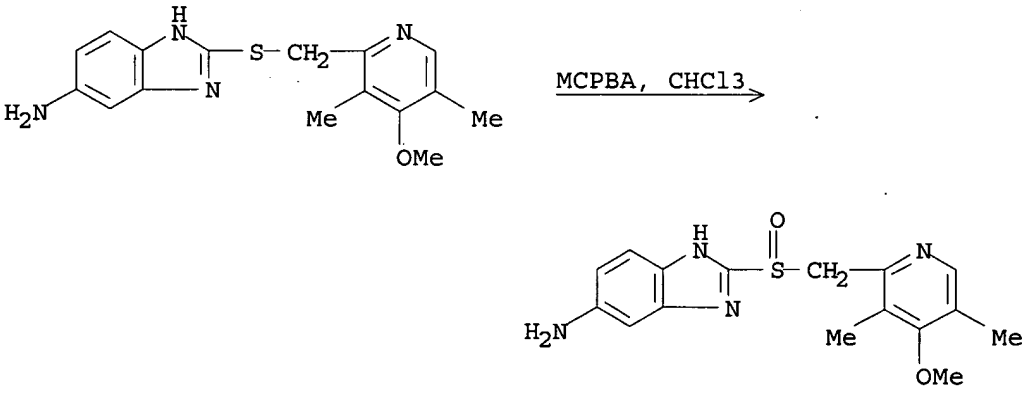
ACCESSION NUMBER:	109:170312 CASREACT
TITLE:	Antisecretory and antiulcer activities of some new 2-(2-pyridylmethylsulfinyl)benzimidazoles
AUTHOR(S):	Cereda, Enzo; Turconi, Marco; Ezhaya, Antoine; Bellora, Elio; Brambilla, Alessandro; Pagani, Ferdinando; Donetti, Arturo
CORPORATE SOURCE:	Dep. Med. Chem. Pharmacol., Ist. De Angeli, Milan, I-20139, Italy
SOURCE:	European Journal of Medicinal Chemistry (1987), 22(6), 527-37 CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE:	Journal
LANGUAGE:	English
GI	



I

AB A series of substituted sulfinylbenzimidazoles e.g., I [R = R2 = H; R1 = NH2, NHAc, NHCO2Et; NHC(S)NHMe; RR1 = COO(CH2)2, R2 = H; R = H, R1R2 = (CH2)3CO] were prepared and tested for gastric anti-secretory activity. Following initial screening, two compds. were tested for anti-ulcer activity. The new compds. showed pharmacol. properties different from those of omeprazole, since they proved to be weak anti-secretory agents displaying nonspecific anti-ulcer activity. Some structural requirements for optimum activity were elucidated.

RX(38) OF 139

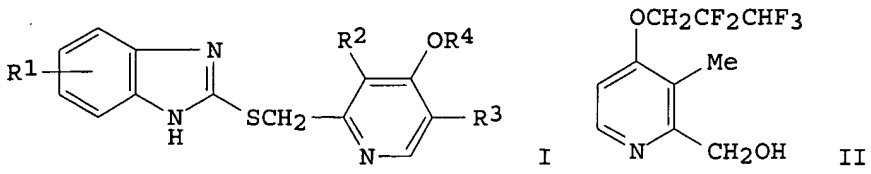


L2 ANSWER 92 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 108:131818 CASREACT
TITLE: Preparation of 2-[(2-pyridylmethyl)thio or -sulfinyl]benzimidazoles as antiulcer agents
INVENTOR(S): Nohara, Akira; Maki, Yoshitaka
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd. , Japan
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. 4,628,098. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4689333	A	19870825	US 1986-937193	19861202
JP 61050978	A	19860313	JP 1984-171069	19840816
JP 02044473	B	19901004		

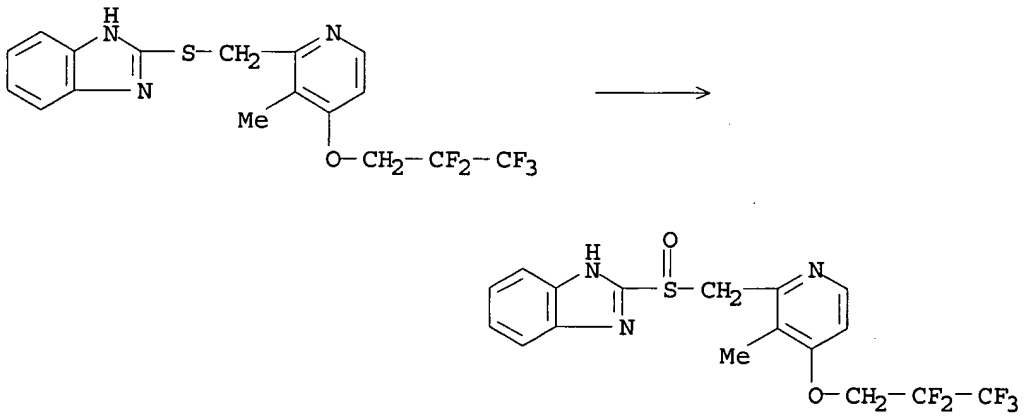
US 4628098 A 19861209 US 1985-760568 19850729
PRIORITY APPLN. INFO.: JP 1984-171069 19840816
US 1985-760568 19850729

GI



AB The title compds. (I; R1 = H, OMe, CF3; R2, R3 = H, Me; R4 = C2-5 fluoroalkyl; n = 0, 1) were prepared and are used for treatment of gastric ulcers or gastritis. 2,3-Dimethyl-4-nitropyridine 1-oxide was alkoxylated with F2CHCF2CH2OH, followed by acetylation and hydrolysis to give pyridinemethanol II. II was chlorinated with SOCl2 and treated with 2-mercaptobenzimidazole to give I (R1 = R3 = H, R2 = Me, R4 = CH2CF2CHF2, n = 0), which was oxidized with 3-ClC6H4C(O)OOH to give I (R1-R4 as before, n = 1). I (R1 = R3 = H, R2 = Me, R4 = CH2CF3, n = 1) (III) had an ED50 of <1.0 mg/kg orally against gastric ulcers in rats. Capsules were prepared each containing III 30, cornstarch 40, lactose 74, hydroxypropylcellulose 6, and MgCO3 50 mg.

RX(3) OF 26



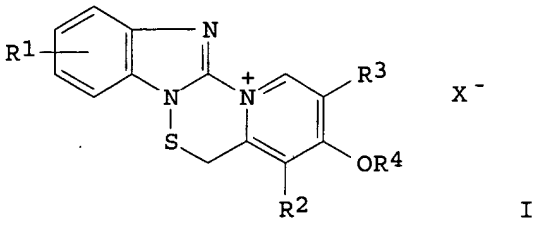
L2 ANSWER 93 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 108:6051 CASREACT
TITLE: Preparation of pyridothiadiazinobenzimidazoles as ulcer inhibitors
INVENTOR(S): Nohara, Akira; Maki, Yoshitaka
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd. , Japan
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 233760	A1	19870826	EP 1987-301243	19870213

EP 233760	B1	19910515		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
CA 1276017	C	19901106	CA 1987-529446	19870211
JP 62277392	A	19871202	JP 1987-29998	19870212
JP 07098825	B	19951025		
US 4769456	A	19880906	US 1987-14352	19870213
PRIORITY APPLN. INFO.:			JP 1986-29569	19860213

OTHER SOURCE(S): MARPAT 108:6051

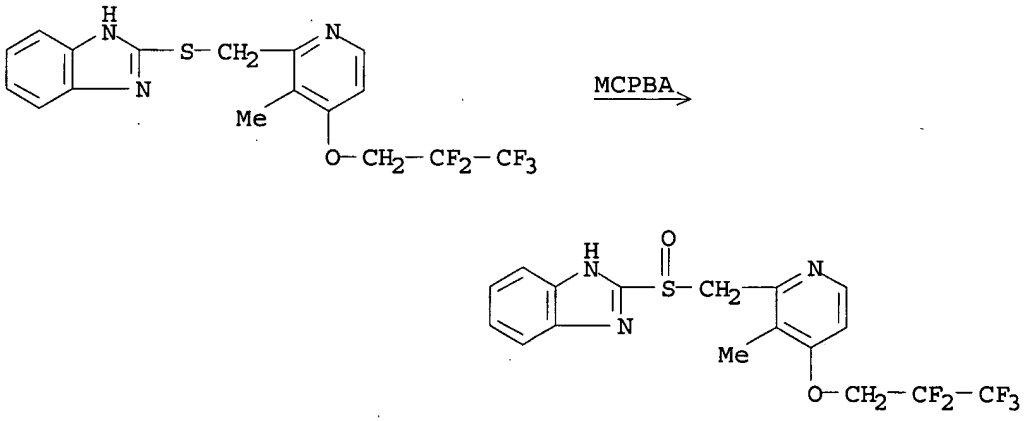
GI



I

AB The title compds. (I; R1 = H, MeO, CF3; R2,R3 = H, Me; R4 = fluoroalkyl; X = pharmaceutically acceptable anion) were prepared as ulcer inhibitors (no data). 2-[[3-Methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methylsulfinyl]benzimidazole and HBF4 in MeOH were heated at 37° to give I(R1 = R3 = H, R4 = CH2CF3)(II).BF4-.

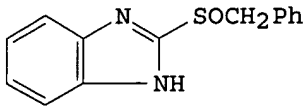
RX(2) OF 2



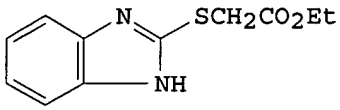
L2 ANSWER 94 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	107:175947 CASREACT
TITLE:	Reaction of 2-(alkylsulfinyl)-, 2-(arylsulfinyl)-, and 2-(aralkylsulfinyl)benzimidazoles with thiols: a convenient synthesis of unsymmetrical disulfides
AUTHOR(S):	Graber, David R.; Morge, Raymond A.; Sih, John C.
CORPORATE SOURCE:	Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE:	Journal of Organic Chemistry (1987), 52(20), 4620-2 CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE:	Journal
LANGUAGE:	English

GI



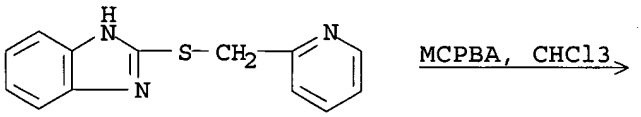
I

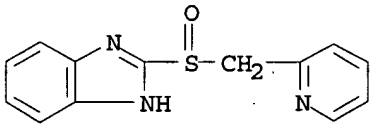


II

AB Unsym. disulfides were prepared under neutral conditions in 52-90% yield by reacting 2-sulfinylbenzimidazoles with thiols. Thus, benzylsulfinylbenzimidazole I was treated with HSCH2CO2Et in EtOH to give 75% PhCH2SSCH2CO2Et. The chief by product of the reaction is the thio ether, e.g., II, of benzimidazole and the reacting thiol.

RX(2) OF 73



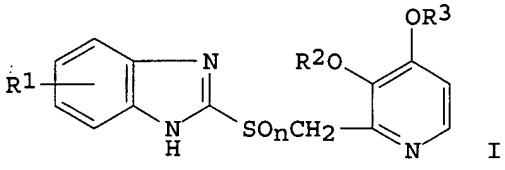


L2 ANSWER 95 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 106:138448 CASREACT
TITLE: Preparation of (pyridylmethylthio)benzimidazoles as antiulcer agents
INVENTOR(S): Nohara, Akira; Maki, Yoshitaka
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd. , Japan
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 208452	A2	19870114	EP 1986-304803	19860623
EP 208452	A3	19880330		
EP 208452	B1	19910918		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
CN 85106134	A	19870304	CN 1985-106134	19850814
CN 1011588	B	19910213		
US 4738975	A	19880419	US 1986-875702	19860618
AT 67494	T	19911015	AT 1986-304803	19860623
DK 8603072	A	19870103	DK 1986-3072	19860627
DK 170819	B1	19960129		
CA 1339819	C	19980414	CA 1986-512760	19860630
HU 43589	A2	19871130	HU 1986-2745	19860701
HU 196997	B	19890228		
CN 86104636	A	19870128	CN 1986-104636	19860702
CN 1018642	B	19921014		
JP 62116576	A	19870528	JP 1986-156824	19860702
JP 06074270	B	19940921		
PRIORITY APPLN. INFO.:			JP 1985-146395	19850702

JP 1985-160457 19850719
EP 1986-304803 19860623

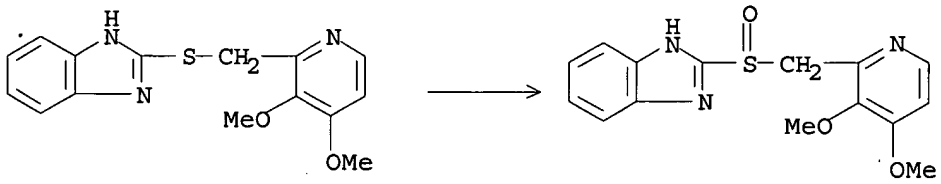
OTHER SOURCE(S): MARPAT 106:138448
GI



I

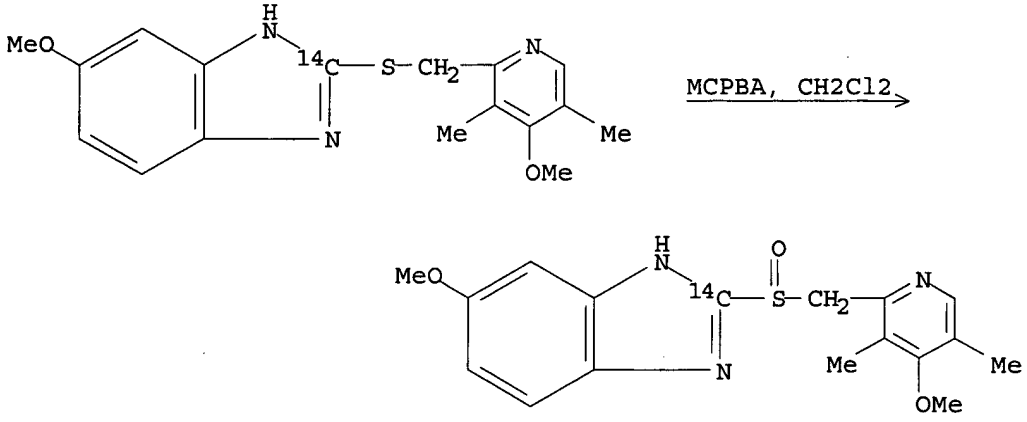
AB The title compds. [I; R1 = H, F, OMe, CF3; R2 = C1-8 alkyl; R3 = C1-8(fluoro)alkyl; n = 0, 1] were prepared as antiulcer agents. 2-Mercaptobenzimidazole K salt reacted with 2-(bromomethyl)-3,4-dimethoxypyridine (preparation given) to give I (R1 = H, R2 = R3 = Me, n = 0) which was oxidized with 3-ClC6H4C(O)OOH to give I (R1 = H, R2 = R3 = Me, n = 1) (II). In rats II inhibited EtOH-induced gastric mucosal injury with an ED50 of 3.2 mg/kg orally.

RX(2) OF 7



L2 ANSWER 96 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 106:84476 CASREACT
TITLE: The preparation of carbon-14-, sulfur-35-, and carbon-13-labeled forms of omeprazole
AUTHOR(S): Crowe, A. M.; Ife, R. J.; Mitchell, M. B.; Saunders, D.
CORPORATE SOURCE: Smith Kline and French Res. Ltd., The Frythe/Welwyn/Hertfordshire, AL6 9AR, UK
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1986), 23(1), 21-33
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Omeprazoles labeled with carbon-13 or -14 at the benzimidazole position, sulfur-35, or carbon-14 at the methylene position (4 compds.) were prepared

RX(3) OF 42



L2 ANSWER 97 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 106:5044 CASREACT

TITLE: Benzimidazoles and their use as stomach secretion inhibitors

INVENTOR(S): Roesner, Manfred; Herling, Andreas W.; Bickel, Martin

PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.

SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

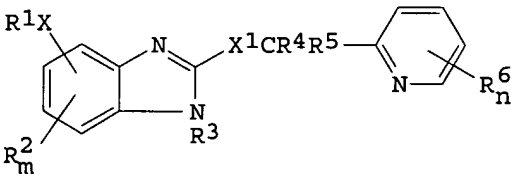
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3509333	A1	19860918	DE 1985-3509333	19850315
EP 198208	A1	19861022	EP 1986-103133	19860308
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ES 552955	A1	19871101	ES 1986-552955	19860313
DK 8601187	A	19860916	DK 1986-1187	19860314
JP 61215388	A	19860925	JP 1986-55177	19860314

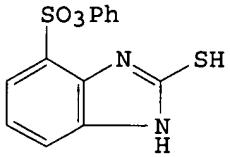
PRIORITY APPLN. INFO.: DE 1985-3509333 19850315

OTHER SOURCE(S): MARPAT 106:5044

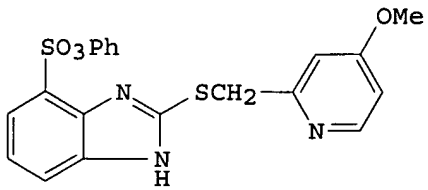
GI



I



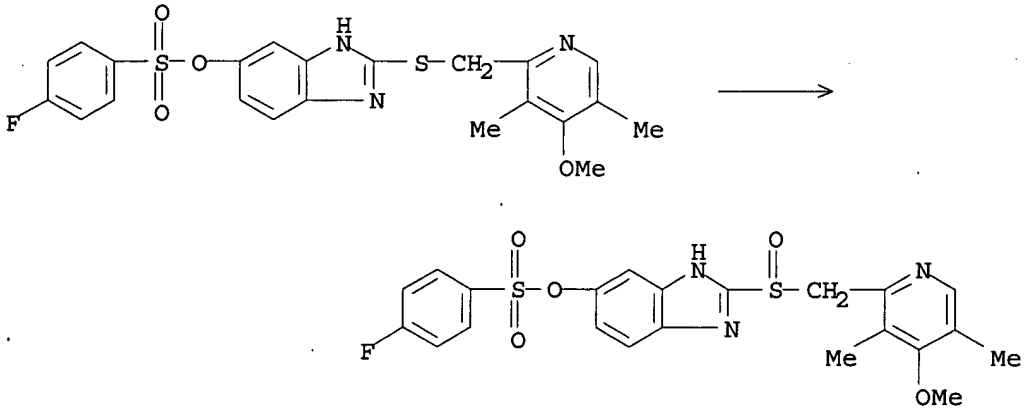
II



III

AB Title compds. [I; m = 0-3; n = 0-4; X = S, SO, SO2, SO3, O3S, SO2NH, NHSO2; X1 = S, SO, SO2; R1 = (substituted) aromatic, heteroarom. group; R2 = halo, cyano, NO2, CF3, alkyl, alkoxy, alkylthio, alkylsulfonyl, etc.; R3 = H, N-protecting group, alkyl, acyl, alkylcarbamoyl; R4, R5 = H, alkyl; R6 = alkyl, alkoxy, alkoxyalkyl, alkoxyalkoxy], useful as inhibitors of stomach secretion (no data), were prepared Thus, PhO3SC6H4(NH2)2-3,4 cyclocondensed with CS2 to give mercaptobenzimidazole II, which reacted with 2-(chloromethyl)-4-methoxypyridine to give (pyridylmethylthio)benzimidazole III.

RX(1) OF 1



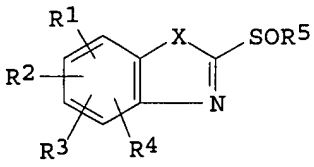
L2 ANSWER 98 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 105:153060 CASREACT
TITLE: Benzimidazolyl benzyl sulfoxides and benzoxazole and benzothiazole analogs
INVENTOR(S): Cox, David; Ingall, Anthony Howard; Suschitzky, John Louis
PATENT ASSIGNEE(S): Fisons PLC, UK
SOURCE: Fr. Demande, 51 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2567123	A1	19860110	FR 1985-10337	19850705
FR 2567123	B1	19910531		
ZA 8505030	A	19860528	ZA 1985-5030	19850603
GB 2161160	A	19860108	GB 1985-16434	19850628
GB 2161160	B	19890524		
EP 174717	A1	19860319	EP 1985-304626	19850628
EP 174717	B1	19920122		
R: AT, DE, NL, SE				
AT 71942	T	19920215	AT 1985-304626	19850628
CA 1341314	C	20011106	CA 1985-485915	19850628
AU 8544441	A	19860109	AU 1985-44441	19850701
AU 580607	B2	19890119		
IL 75687	A	19900319	IL 1985-75687	19850701
DK 8503018	A	19860107	DK 1985-3018	19850702
DK 174021	B1	20020422		
CN 85106252	A	19860610	CN 1985-106252	19850702

CN 1004756	B	19890712		
FI 8502622	A	19860107	FI 1985-2622	19850703
FI 89046	B	19930430		
FI 89046	C	19930810		
BE 902818	A1	19860106	BE 1985-215301	19850704
CH 666265	A5	19880715	CH 1985-2873	19850704
NO 8502729	A	19860107	NO 1985-2729	19850705
NO 168355	B	19911104		
NO 168355	C	19920212		
JP 61056168	A	19860320	JP 1985-146903	19850705
JP 2564509	B2	19961218		
ES 544897	A1	19861201	ES 1985-544897	19850705
HU 39730	A2	19861029	HU 1985-4489	19851125
HU 198695	B	19891128		
DD 242614	A5	19870204	DD 1985-283389	19851128
SU 1524807	A3	19891123	SU 1985-3979903	19851128
BR 8506098	A	19870630	BR 1985-6098	19851205
PRIORITY APPLN. INFO.:			GB 1984-17271	19840706
			GB 1984-17272	19840706
			GB 1984-19738	19840802
			GB 1984-24346	19840926
			GB 1984-24347	19840926
			GB 1984-24350	19840926
			GB 1984-24351	19840926
			GB 1984-30163	19841129
			GB 1985-9406	19850412
			EP 1985-304626	19850628

OTHER SOURCE(S): MARPAT 105:153060

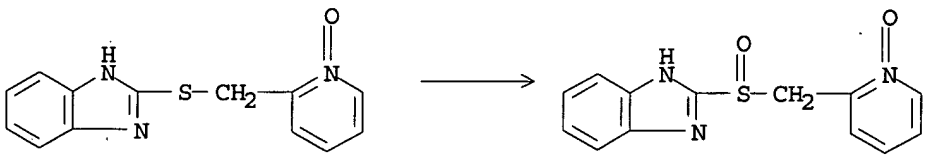
GI



I

AB Title compds. I (X = O, S, NH, acylimino, etc.; R1-R4 = H, halo, alkoxy, alkyl, fluoroalkyl, alkanoyl, NO2, etc.; R5 = N-, O-, or S-containing nucleophilic group) were prepared as gastric secretion inhibitors (no data). 2-Mercaptobenzothiazole was S-alkylated by 2-Me2NC6H4CH2Cl.HCl, and the sulfide product was oxidized to give I (X = NH, R1-R4, = H, R5 = 2-Me2NC6H4CH2).

RX(29) OF 43



L2 ANSWER 99 OF 104 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 105:97470 CASREACT

TITLE: Benzimidazole derivatives

INVENTOR(S): Nohara, Akira; Maki, Yoshitaka

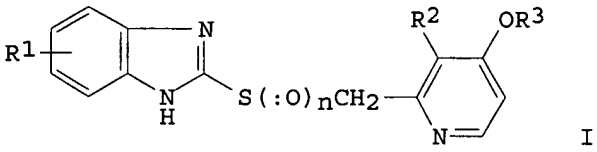
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd. , Japan

10/542,268

SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 175464	A1	19860326	EP 1985-305459	19850731
EP 175464	B1	19920318		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 61050979	A	19860313	JP 1984-171070	19840816
JP 04075914	B	19921202		
AT 73796	T	19920415	AT 1985-305459	19850731
CA 1256878	A1	19890704	CA 1985-488661	19850814
US 4727150	A	19880223	US 1987-16951	19870220
PRIORITY APPLN. INFO.:			JP 1984-171070	19840816
			US 1985-760567	19850729
			EP 1985-305459	19850731

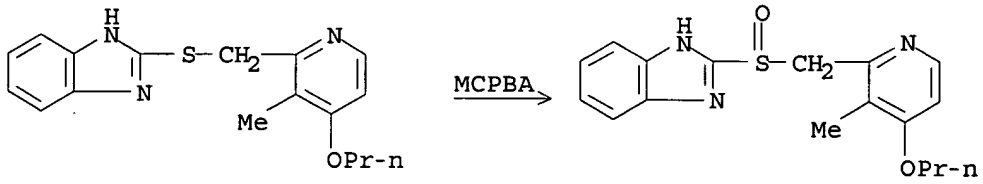
OTHER SOURCE(S): MARPAT 105:97470
GI



I

AB Benzimidazole derivs. I (R1 = H, F, MeO, F3C; R2 = H, Me; R3 = C3-8 alkyl; n = 0, 1) are prepared for prophylaxis and therapy of ulcers and gastritis. For example, 2,3-dimethyl-4-nitropyridine 1-oxide was converted to 2,3-dimethyl-4-propoxypyridine 1-oxide in PrOH-K2CO3 at 80°, then to 2-hydroxymethyl-3-methyl-4-propoxypyridine in Ac2O-H2O4 at 100° followed by KOH. Reaction with SOCl2 and 2-mercaptobenzimidazole yielded I (R1 = H; R2 = Me; R3 = Pr; n = 0) (II), which was converted to the sulfinyl compound (II; n = 1) with m-chloroperbenzoic acid. II showed an oral ID50 of 12.5 mg/kg in protecting the gastric mucosa of rats from EtOH-inudced ulcers.

RX(5) OF 19



L2 ANSWER 100 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 105:78880 CASREACT
TITLE: Acid activation of (H+-K+)-ATPase inhibiting 2-(2-pyridylmethylsulfinyl)benzimidazoles: isolation and characterization of the thiophilic 'active principle' and its reactions

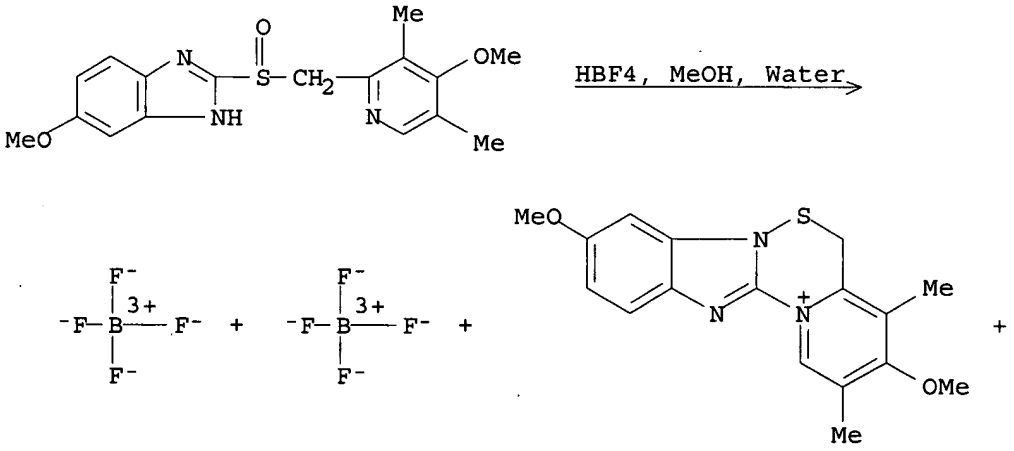
10/542,268

AUTHOR(S): Figala, V.; Klemm, K.; Kohl, B.; Krueger, U.; Rainer, G.; Schaefer, H.; Senn-Bilfinger, J.; Sturm, E.
CORPORATE SOURCE: Byk Gulden Lomberg, Chem. Fabrik G.m.b.H., Konstanz, Fed. Rep. Ger.
SOURCE: Journal of the Chemical Society, Chemical Communications (1986), (2), 125-7
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

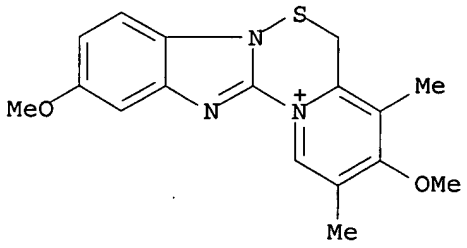
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB As a model for the inhibition of (H+-K+)-ATPase from the acidic luminal side, the reactions of benzimidazoles I (R = OMe, R1 = R2 = Me; R = CF3, R1 = Me, H, R2 = H; R = R2 = H, R1 = Me) with HS(CH2)2OH (II) in acid were studied. Treatment of I with II in 0.1M HCl gave pyridiniobenzimidazolides III (R-R2 as before). Reaction of I with HBF4 in H2O-MeOH at -5° gave the tetracyclic compds. IV (R = OMe, R1 = R2 = Me; R = CF3, H, R1 = Me, R2 = H) as regioisomeric mixts. IV reacted almost instantaneously with II to give III. Derivs. of I unable to form the almost planar structure IV showed no biol. activity. Thus, IV is the active principle in the class of benzimidazole drugs. The structures of III (R = CF3, R1 = Me, R2 = H) and IV (R = R2 = H, R1 = Me) were determined by x-ray crystallog.

RX(2) OF 15



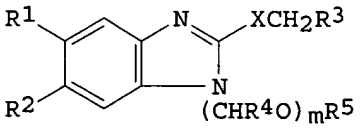
RX(2) OF 15

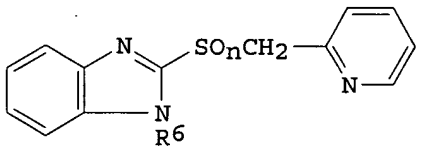


L2 ANSWER 101 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 105:60604 CASREACT
TITLE: 2-(Pyridylmethylsulfinyl)benzimidazoles
INVENTOR(S): Sih, John Charles; Cho, Moo Jung
PATENT ASSIGNEE(S): Upjohn Co. , USA
SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 176308	A2	19860402	EP 1985-306600	19850917
EP 176308	A3	19870401		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
AU 8546690	A	19860410	AU 1985-46690	19850827
AU 568441	B2	19871224		
ZA 8506671	A	19860430	ZA 1985-6671	19850830
JP 61078784	A	19860422	JP 1985-206779	19850920
DK 8504302	A	19860325	DK 1985-4302	19850923
FI 8503649	A	19860325	FI 1985-3649	19850923
ES 547226	A1	19861116	ES 1985-547226	19850923
US 4873337	A	19891010	US 1987-81583	19870803
PRIORITY APPLN. INFO.:			US 1984-653999	19840924
			US 1984-682980	19841218
			US 1985-761239	19850731

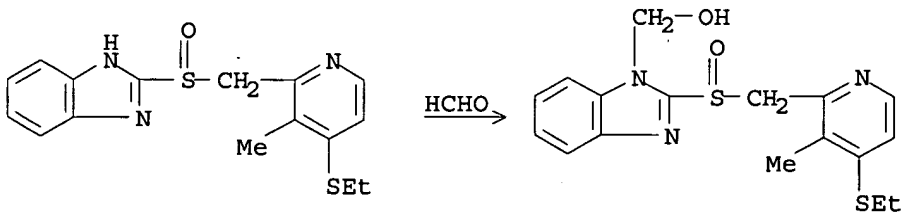
OTHER SOURCE(S): MARPAT 105:60604
GI


I


II

AB The title compds. [I; R1, R2 = H, alkyl, alkoxy, CF3, alkanoyl, alkoxycarbonyl; R3 = substituted 2-pyridinyl, condensed pyridinyl; R4 = H, alkyl; R5 = H; alkyl, (un)substituted alkanoyl, Bz, CO2H; X = S, SO; m = 0, 1] were prepared as gastric secretion inhibitors. Thus, 10 g 2-[(2-pyridinylmethyl)thio]benzimidazole (II; R6 = H, n = 0) was hydroxymethylated with H2CO to give II (R6 = HOCH2, n = 0). This was acetylated and oxidized to give sulfoxide II (R6 = AcOCH2, n = 1) (III). In rats III had an ED50 of 5 mg/kg orally in the gastric antisecretory test.

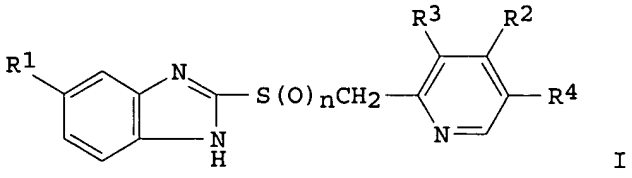
RX(5) OF 52



L2 ANSWER 102 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 104:19586 CASREACT
TITLE: 2-(Pyridylmethylthio)benzimidazoles and 2-(pyridylmethylsulfinyl)benzimidazoles
INVENTOR(S): Sih, John Charles
PATENT ASSIGNEE(S): Upjohn Co. , USA
SOURCE: Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 150586	A2	19850807	EP 1984-308376	19841203
EP 150586	A3	19850828		
EP 150586	B1	19910508		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4575554	A	19860311	US 1984-648118	19840906
IL 73433	A	19881130	IL 1984-73433	19841105
ZA 8408746	A	19850731	ZA 1984-8746	19841108
AU 8435643	A	19850613	AU 1984-35643	19841119
AU 571907	B2	19880428		
FI 8404755	A	19850606	FI 1984-4755	19841203
FI 83418	B	19910328		
FI 83418	C	19910710		
DK 8405775	A	19850606	DK 1984-5775	19841204
NO 8404836	A	19850606	NO 1984-4836	19841204
NO 164473	B	19900702		
NO 164473	C	19901010		
JP 60139689	A	19850724	JP 1984-257268	19841204
JP 05072392	B	19931012		
ES 538249	A1	19860116	ES 1984-538249	19841204
US 4619997	A	19861028	US 1985-812224	19851223
PRIORITY APPLN. INFO.:			US 1983-558087	19831205
			US 1984-648118	19840906

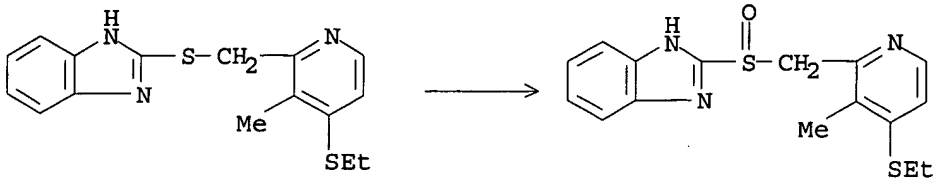
OTHER SOURCE(S): MARPAT 104:19586
GI



I

AB Gastric antisecretory and cytoprotective (no data) title compds. [I; R1 = H, Me, CF3, MeO; R2 = amino, 1-piperidinyl, 4-morpholinyl, 4-methyl-1-piperazinyl, 1-pyrrolidinyl, R5Z; R3, R4 = H, alkyl; R5 = alkyl, alkenyl, cycloalkyl, (un)substituted Ph, PhCH2; Z = O, S; n = 0, 1] (56 compds.) were prepared by several methods, e.g., by the condensation of 2-(chloromethyl)pyridines with benzimidazole-2-thiols to give I (n = 0), followed by oxidation with 3-ClC6H4C(O)OOH to give I (n = 1).

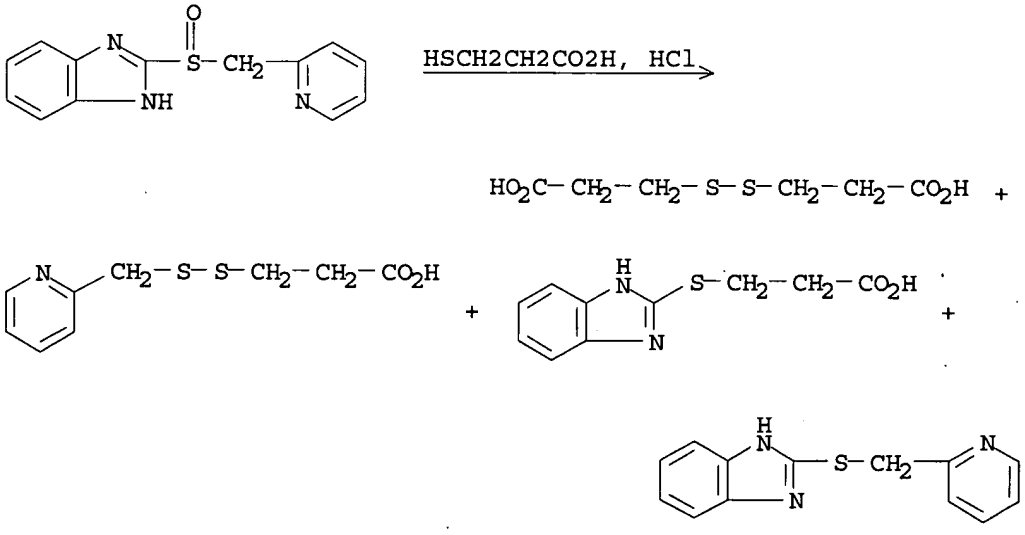
RX(1) OF 4



L2 ANSWER 103 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 103:87431 CASREACT
TITLE: 2-[(2-Pyridylmethyl)sulfinyl]benzimidazoles: acid sensitive suicide inhibitors of the proton transport system in the parietal cell
AUTHOR(S): Rackur, G.; Bickel, M.; Fehlhaber, H. W.; Herling, A.; Hitzel, V.; Lang, H. J.; Roesner, M.; Weyer, R.
CORPORATE SOURCE: Hoechst A.-G., Frankfurt/Main, D-6230, Fed. Rep. Ger.
SOURCE: Biochemical and Biophysical Research Communications (1985), 128(1), 477-84
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In acid medium, 2-[(2-pyridylmethyl)sulfinyl]benzimidazoles, selective inhibitors of the H+/K+-ATPase in the parietal cells of the stomach, undergo protonation of the sulfoxide and subsequent elimination of water to form a sulfenium ion or a chemical equivalent thereof. If no external nucleophiles are present, rearrangement takes place. In the presence of mercaptans, the sulfenium ion is trapped giving rise to a variety of products. On the basis of these results, a mechanistic scheme is proposed for the inactivation of the H+/K+-ATPase by these compds.

RX(6) OF 8



L2 ANSWER 104 OF 104 CASREACT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 100:44878 CASREACT
TITLE: Antiulcer and gastric antisecretory activity of a

series of thioethers and related sulfoxides

AUTHOR(S): Beattie, Doreen E.; Crossley, Roger; Dickinson, Kay H.; Dover, Gillian M.

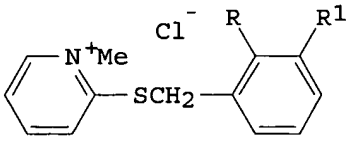
CORPORATE SOURCE: Wyeth Lab., Inst. Med. Res., Maidenhead/Berkshire, SL6 0PH, UK

SOURCE: European Journal of Medicinal Chemistry (1983), 18(3), 277-85
CODEN: EJMCA5; ISSN: 0009-4374

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

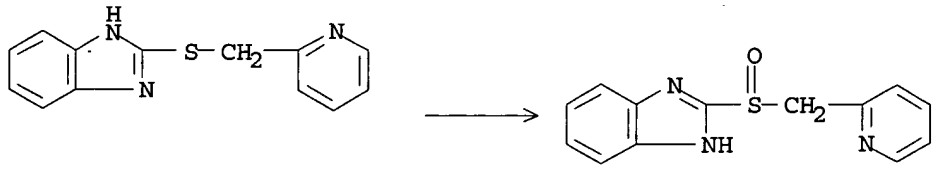


I, R=H, R^1=Cl

II, R=F, R^1=H

AB A series of thioethers containing a pyridinium moiety were prepared and tested for gastric antisecretory and antiulcer activity in laboratory animals. Following initial screening, 2 compds., 2-(3-chlorobenzylthio)-1-methylpyridinium chloride (I) [77148-72-2] and 2-(2-fluorobenzylthio)-1-methylpyridinium chloride (II) [77155-89-6], were investigated further. By modification of substituent groups, some separation of antiulcer and antisecretory activity was achieved. Subsequently it was found that the pyridinium moiety could be replaced and a number of related thioethers and sulfoxides were synthesized and were also found to be active. A wide range of structural variations were found to be possible with retention of activity.

RX(6) OF 99



2 HCl

39%

=>